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(54) Title: 7–ALKYL– AND CYCLOALKYL–SUBSTITUTED IMIDAZOTRIAZINONES

(54) Bezeichnung: 7–ALKYL– UND CYCLOALKYL–SUBSTITUIERTE IMIDAZOTRIAZINONE

(57) Abstract

The invention relates to 7–alkyl– and cycloalkyl–substituted imidazotriazinones, a method for preparing them and using them as drugs, especially as inhibitors of cGMP–metabolising phosphodiesterases.

(57) Zusammenfassung

Die vorliegende Erfindung betrifft 7–Alkyl– und Cycloalkyl–substituierte Imidazotriazinone, Verfahren zu ihrer Herstellung und ihre Verwendung als Arzneimittel, insbesondere als Inhibitoren cGMP–metabolisierender Phosphodiesterasen.

LEDIGLICH ZUR INFORMATION

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Niewöhner et al.

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(45) **Date of Patent: Nov. 5, 2002**

(54) **7-ALKYL- AND CYCLOALKYL-SUBSTITUTED IMIDAZOTRIAZINONES**

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(52) **U.S. Cl.** **514/243**; 544/184

(58) **Field of Search** 544/184; 514/243

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(57) **ABSTRACT**

The present invention relates to 7-alkyl- and cycloalkyl-substituted imidazotriazinones, to processes for their preparation and to their use as medicaments, in particular as inhibitors of cGMP-metabolizing phosphodiesterases.

11 Claims, No Drawings

7-ALKYL- AND CYCLOALKYL-SUBSTITUTED IMIDAZOTRIAZINONES

The present invention relates to 7-alkyl- and cycloalkyl-substituted imidazotriazinones, to processes for their preparation and to their use as medicaments, in particular as inhibitors of cGMP-metabolizing phosphodiesterases.

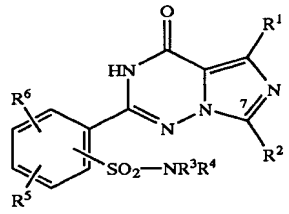
The published specification DE-28 11 780 describes imidazotriazines as bronchodilators having spasmolytic activity and inhibitory activity against phosphodiesterases which metabolize cyclic adenosine monophosphate (cAMP-PDEs, nomenclature according to Beavo: PDE-III and PDE-IV). An inhibitory action against phosphodiesterases which metabolize cyclic guanosine monophosphate (cGMP-PDEs, nomenclature according to Beavo and Reifsnyder (Trends in Pharmacol. Sci. 11, 150–155, 1990) PDE-I, PDE-II and PDE-V) has not been described. Compounds having a sulphonamide group in the aryl radical in the 2 position are not claimed. Furthermore, FR 22 13 058, CH-59 46 71, DE-22 55 172, DE-23 64 076 and EP-000 9384 describe imidazotriazinones which do not have a substituted aryl radical in the 2 position and are likewise said to be bronchodilators having cAMP-PDE-inhibitory action.

The compounds according to the invention are potent inhibitors either of one or of more of the phosphodiesterases which metabolize cyclic guanosine 3',5'-monophosphate (cGMP-PDEs). According to the nomenclature of Beavo and Reifsnyder (Trends in Pharmacol. Sci. 11, 150–155, 1990) these are the phosphodiesterase isoenzymes PDE-I, PDE-II and PDE-V.

An increase in the cGMP concentration can lead to beneficial antiaggregatory, antithrombotic, antiprolific, antivasospastic, vasodilative, natriuretic and diuretic effects. It can influence the short- or long-term modulation of muscular and cardiac inotropy, of the pulse and of cardiac conduction (J. C. Stoclet, T. Keravis, N. Komas and C. Lugnier, Exp. Opin. Invest. Drugs (1995), 4 (11), 1081–1100).

The present invention, accordingly, provides 7-alkyl- and cycloalkyl-substituted imidazotriazinones of the general formula (I)

(I)



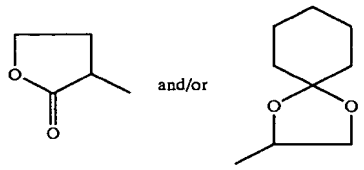
in which

R^1 represents straight-chain or branched alkyl having up to 4 carbon atoms,

R^2 represents straight-chain alkyl having at least 5 carbon atoms or branched alkyl having at least 3 carbon atoms, or represents cycloalkyl having 3 to 10 carbon atoms,

R^3 and R^4 are identical or different and represent hydrogen, or represent straight-chain or branched alkenyl having up to 8 carbon atoms, or represent a straight-chain or branched alkyl chain having up to 10 carbon atoms which is optionally interrupted by an oxygen atom and which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of trifluoromethyl, trifluoromethoxy,

hydroxyl, halogen carboxyl, benzyloxycarbonyl, straight-chain or branched alkoxy, alkoxycarbonyl and alkylthio having in each case up to 6 carbon atoms and/or by radicals of the formulae $—SO_3H$, $—(A)_a—NR^7R^8$, $—O—CO—NR^{7'}R^{8'}$, $—S(O)_b—R^9$, $HN=SO—R^{9'}$, $—P(O)(OR^{10})(OR^{11})$,



and/or

in which

a and b are identical or different and represent a number 0 or 1,

A represents a radical CO or SO_2,

R^7, $R^{7'}$, R^8 and $R^{8'}$ are identical or different and represent hydrogen, or represent cycloalkyl having 3 to 8 carbon atoms, aryl having 6 to 10 carbon atoms, a 5- to 6-membered unsaturated, partially unsaturated or saturated, optionally benzo-fused heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O, where the ring systems listed above are optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, nitro, trifluoromethyl, trifluoromethoxy, carboxyl, halogen, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 6 carbon atoms or by a group of the formula $—(SO_2)_c—NR^{12}R^{13}$,

in which

c represents a number 0 or 1,

R^{12} and R^{13} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 5 carbon atoms,

or

R^7, $R^{7'}$, R^8 and $R^{8'}$ represent straight-chain or branched alkoxy having up to 6 carbon atoms, or represent straight-chain or branched alkyl having up to 8 carbon atoms which is optionally mono- or polysubstituted by identical or different substituents from the group consisting of hydroxyl, halogen, aryl having from 6 to 10 carbon atoms, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 6 carbon atoms or by a group of the formula $—(CO)_d—NR^{14}R^{15}$,

in which

R^{14} and R^{15} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms. and

d represents a number 0 or 1, or

R^7 and R^8 and/or $R^{7'}$ and $R^{8'}$ together with the nitrogen atom form a 5- to 7-membered saturated heterocycle which may optionally contain a further heteroatom from the group consisting of S and O or a radical of the formula $—NR^{16}$,

in which

R^{16} represents hydrogen, aryl having 6 to 10 carbon atoms, or straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally substituted by hydroxyl,

R^9 and $R^{9'}$ are identical or different and represent aryl having 6 to 10 carbon atoms or benzyl, or represent straight-chain or branched alkyl having up to 4 carbon atoms,

R^{10} and R^{11} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms,

and/or the alkyl chain listed above under R^3/R^4 is optionally substituted by cycloalkyl having 3 to 8 carbon atoms, aryl having 6 to 10 carbon atoms or by a 5- to 7-membered partially unsaturated, saturated or unsaturated, optionally benzo-fused heterocycle which may contain up to 4 ring heteroatoms from the group consisting of S, N, O or a radical of the formula —NR^{17}, where the alkyl chain may optionally also be attached via a ring nitrogen atom,

in which

R^{17} represents hydrogen, hydroxyl, formyl, trifluoromethyl, straight-chain or branched acyl or alkoxy having in each case up to 4 carbon atoms, or represents straight-chain or branched alkyl having up to 6 carbon atoms which is optionally mono- to polysubstituted by identical or different substituents from the group consisting of hydroxyl and straight-chain or branched alkoxy having up to 6 carbon atoms,

and where aryl and the heterocycle are optionally mono- to trisubstituted by identical or different substituents from the group consisting of nitro, halogen, —SO_3H, straight-chain or branched monohydroxy-substituted alkyl, alkylthio or alkoxy having in each case up to 6 carbon atoms, hydroxyl, trifluoromethyl, trifluoromethoxy and/or by a radical of the formula —$(SO_2)_e$—$R^{18}R^{19}$,

in which

e represents a number 0 or 1,

R^{18} and R^{19} are identical or different and represent hydrogen, phenyl, benzyl or straight-chain or branched alkyl or acyl having in each case up to 6 carbon atoms,

and/or

R^3 or R^4 represent radicals of the formulae —$NR^{20}R^{21}$ or —(O)—E—$NR^{22}R^{23}$,

in which

R^{20} and R^{21} have the meaning of R^{18} and R^{19} given above and are identical to or different from this meaning, or together with the nitrogen atom form a 5- or 6-membered saturated heterocycle having a further ring heterocycle from the group consisting of S and O or a radical —NR^{24},

in which

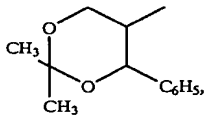
R^{24} has the meaning of R^{16} given above and is identical to or different from this meaning,

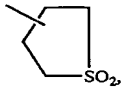
E is a straight-chain alkylene group having up to 5 carbon atoms,

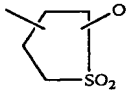
R^{22} and R^{23} have the meaning of R^{18} and R^{19} given above and are identical to or different from this meaning,

and/or

R^3 or R^4 represent radicals of the formulae







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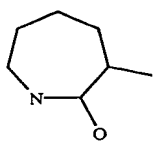


or represent cycloalkyl having 3 to 8 carbon atoms, aryl having 6 to 10 carbon atoms or represent a 5- to 7-membered partially unsaturated, saturated and unsaturated, optionally benzo-fused heterocycle which may contain up to 4 heteroatoms from the group consisting of S, N, O or a radical of the formula —NR^{25} which may optionally also be attached via a ring nitrogen atom,

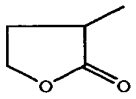
in which

R^{25} has the meaning of R^{16} given above and is identical to or different from this meaning, or represents carboxyl, formyl or straight-chain or branched acyl having up to 5 carbon atoms,

and where cycloalkyl, aryl and/or the heterocycle are optionally mono- to trisubstituted by identical or different substituents from the group consisting of halogen, trifluoromethyl, trifluoromethoxy, carboxyl, straight-chain or branched acyl or alkoxycarbonyl having in each case up to 6 carbon atoms, nitro and/or by groups of the formulae —SO_3H, —OR^{26}, $(SO_2)_fNR^{27}R^{28}$, —$P(O)(OR^{29})(OR^{30})$,

in which

R^{26} represents a radical of the formula



represents cycloalkyl having 3 to 7 carbon atoms, or hydrogen or straight-chain or branched alkyl having up to 5 carbon atoms which is optionally substituted by cycloalkyl having 3 to 7 carbon atoms, straight-chain or branched alkoxy or alkoxycarbonyl having in each case up to 6 carbon atoms, hydroxyl, carboxyl or phenyl, which for its part may be mono- to trisubstituted by identical or different substituents from the group consisting of straight-chain or branched alkoxy having up to 4 carbon atoms, hydroxyl and halogen,

f is a number 0 or 1,

R^{27} and R^{28} have the meaning of R^{18} and R^{19} given above and are identical to or different from this meaning or represent a radical of the formula —CO—NH_2,

R^{29} and R^{30} have the meaning of R^{10} and R^{11} given above and are identical to or different from this meaning,

and/or cycloalkyl, aryl and/or the heterocycle are optionally substituted by straight-chain or branched alkyl having up to 6 carbon atoms which is optionally substituted by hydroxyl, carboxyl, by a 5- to 7-membered heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O or by groups of the formulae —SO_2—R^{31}, $P(O)(OR^{32})(OR^{33})$ or —$NR^{34}R^{35}$,

in which

R^{31} is hydrogen or has the meaning of R^9 given above and is identical to or different from this meaning,

R^{32} and R^{33} have the meaning of R^{10} and R^{11} given above and are identical to or different from this meaning,

R^{34} and R^{35} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms which is optionally substituted by hydroxyl or straight-chain or branched alkoxy having up to 4 carbon atoms, or

R^{34} and R^{35} together with the nitrogen atom form a 5- to 6-membered saturated heterocycle which may contain a further heteroatom from the group consisting of S and O or a radical of the formula —NR^{36}, in which

R^{36} has the meaning of R^{16} given above and is identical to or different from this meaning,

or

R^3 and R^4 together with the nitrogen atom form a 5- to 7-membered unsaturated or saturated or partially unsaturated, optionally benzo-fused heterocycle which may optionally contain up to 3 heteroatoms from the group consisting of S, N, O or a radical of the formula —NR^{37},

in which

R^{37} represents hydrogen, hydroxyl, formyl, trifluoromethyl, straight-chain or branched acyl, alkoxy or alkoxycarbonyl having in each case up to 4 carbon atoms, or represents cycloalkyl having 3 to 8 carbon atoms, or represents straight-chain or branched alkyl having up to 6 carbon atoms which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, trifluoromethyl, pyridyl, carboxyl, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 6 carbon atoms,

or

R^{37} represents a radical of the formula —$(CO)_g$—G,

in which

g represents a number 0 or 1,

G represents aryl having 6 to 10 carbon atoms or a 5- to 6-membered aromatic heterocycle having up to 4 heteroatoms from the group consisting of S, N and/or O, where the ring systems listed above are optionally mono- to trisubstituted by identical or different substituents from the group consisting of halogen, straight-chain or branched alkoxy, alkyl or alkylthio having in each case up to 6 carbon atoms, hydroxyl and trifluoromethyl,

and the heterocycle mentioned under R^3 and R^4, formed via the nitrogen, is optionally mono- to trisubstituted, optionally also geminally, by identical or different substituents from the group consisting of hydroxyl, formyl, carboxyl, straight-chain or branched acyl and alkoxycarbonyl having in each case up to 6 carbon atoms and groups of the formulae —$P(O)(OR^{38})(OR^{39})$ and —$(CO)_g$—$NR^{40}R^{41}$,

in which

R^{38} and R^{39} have the meaning of R^{10} and R^{11} given above and are identical to or different from this meaning,

g represents a number 0 or 1,

and

R^{40} and R^{41} are identical or different and have the meaning of R^{18} and R^{19} given above,

and/or the heterocycle mentioned under R^3 and R^4, formed via the nitrogen, is optionally substituted by straight-chain or branched alkyl having up to 6 carbon atoms which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, halogen, carboxyl, cycloalkyl or cycloalkyloxy having in each case 3 to 8 carbon atoms, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 6 carbon atoms or by a radical of the formula —SO_3H, —$NR^{42}R^{43}$ or $P(O)OR^{44}OR^{45}$,

in which

R^{42} and R^{43} are identical or different and represent hydrogen, phenyl, carboxyl, benzyl or straight-chain or branched alkyl or alkoxy having in each case up to 6 carbon atoms,

R^{44} and R^{45} are identical or different and have the meaning of R^{10} and R^{11} given above,

and/or the alkyl is optionally substituted by benzyloxy or aryl having 6 to 10 carbon atoms, which for its part may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, hydroxyl, straight-chain or branched alkoxy or alkylthio having in each case up to 6 carbon atoms, or by a group of the formula —$NR^{42'}R^{43'}$,

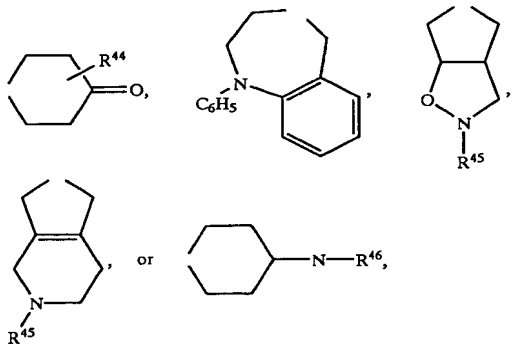
in which

$R^{42'}$ and $R^{43'}$ have the meaning of R^{42} and R^{43} given above and are identical to or different from this meaning,

and/or the heterocycle mentioned under R^3 and R^4, formed via a nitrogen atom, is optionally substituted by aryl having 6 to 10 carbon atoms or by a 5- to 7-membered saturated, partially unsaturated or unsaturated heterocycle having up to 3 ring heteroatoms from the group consisting of S, N and/or O, optionally also attached via an N function, where the ring systems for their part may be substituted by halogen, hydroxyl or by straight-chain or branched alkyl, alkylthio or alkoxy having in each case up to 6 carbon atoms,

or

R^3 and R^4 together with the nitrogen atom form radicals of the formulae



in which

R^{44} represents hydrogen or straight-chain or branched alkyl or alkoxycarbonyl having in each case up to 6 carbon atoms,

R^{45} and $R^{45'}$ are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms,

R^{46} represents hydroxyl or straight-chain or branched alkoxy having up to 6 carbon atoms,

R^5 and R^6 are identical or different and represent hydrogen, straight-chain or branched alkyl having up to

6 carbon atoms, hydroxy or represents straight-chain or branched alkoxy having up to 6 carbon atoms,

and their salts and isomeric forms.

The compounds according to the invention may exist in stereoisomeric forms which are either like image and mirror image (enantiomers), or which are not like image and mirror image (diastereomers). The invention relates both to the enantiomers or diastereomers and to their respective mixtures. The racemic forms can, just like the diastereomers, be separated in a known manner into the stereoisomerically uniform constituents.

The substances according to the invention may also be present as salts. In the context of the invention, preference is given to physiologically acceptable salts.

Physiologically acceptable salts can be salts of the compounds according to the invention with inorganic or organic acids. Preference is given to salts with inorganic acids, such as, for example, hydrochloric acid, hydrobromic acid, phosphoric acid or sulphuric acid, or to salts with organic carboxylic or sulphonic acids, such as, for example, acetic acid, maleic acid, fumaric acid, malic acid, citric acid, tartaric acid, lactic acid, benzoic acid, or methanesulphonic acid, ethanesulphonic acid, phenylsulphonic acid, toluenesulphonic acid or naphthalenedisulphonic acid.

Physiologically acceptable salts can also be metal or ammonium salts of the compounds according to the invention. Particular preference is given to, for example, sodium, potassium, magnesium or calcium salts, and also to ammonium salts which are derived from ammonia or organic amines, such as, for example, ethylamine, di- or triethylamine, di- or triethanolamine, dicyclohexylamine, dimethylaminoethanol, arginine, lysine, ethylenediamine or 2-phenylethylamine.

In the context of the invention and depending on the various substituents, optionally benzo-fused heterocycle generally represents an aromatic, saturated, partially unsaturated or unsaturated 5- to 7-membered or 5- to 6-membered heterocycle which may contain up to 4 heteroatoms from the group consisting of S, N and O. Examples which may be mentioned are: azepine, diazepine, indolyl, isoquinolyl, quinolyl, benzo[b]thiophene, benzo[b]furanyl, pyridyl, thienyl, tetrahydrofuranyl, tetrahydropyranyl, furyl, pyrrolyl, thiazolyl, triazolyl, tetrazolyl, isoxazolyl, imidazolyl, morpholinyl, thiomorpholinyl, pyrrolidinyl, piperazinyl, N-methylpiperazinyl or piperidinyl. Preference is given to quinolyl, furyl, pyridyl, thienyl, piperidinyl, pyrrolidinyl, piperazinyl, azepine, diazepine, thiazolyl, triazolyl, tetrazolyl, tetrahydrofuranyl, tetrahydropyranyl, morphholinyl and thiomorpholinyl.

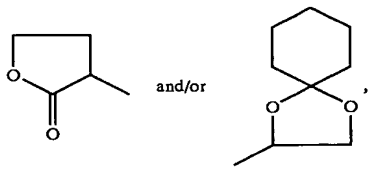
Preference is given to compounds of the general formula (I) according to the invention

in which

represents straight-chain or branched alkyl having up to 3 carbon atoms,

R^2 represents straight-chain alkyl having 5 to 15 carbon atoms or branched alkyl having 3 to 15 carbon atoms, or represents cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl or cyclooctyl,

R^3 and R^4 are identical or different and represent hydrogen, or represent straight-chain or branched alkenyl having up to 4 carbon atoms, or represent a straight-chain or branched alkyl chain having up to 6 carbon atoms which is optionally interrupted by an oxygen atom and which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, carboxyl, straight-chain or branched alkoxy, alkoxycarbonyl and alkylthio having in each case up to 4 carbon atoms and/or by radicals of the formulae $-SO_3H$, $-(A)_a-NR^7R^8$, $-O-C-NR^{7'}R^{8'}$, $-S(O)_b-R^9$, $HN=SO-R^{9'}$, $-P(O)(OR^{10})(OR^{11})$,



in which

a and b are identical or different and represent a number 0 or 1,

A represents a radical CO or SO_2,

R^7, $R^{7'}$, R^8 and $R^{8'}$ are identical or different and represent hydrogen, or represent phenyl, naphthyl, or pyridyl, where the ring systems listed above are optionally mono- to disubstituted by identical or different substituents from the group consisting of hydroxyl, nitro, trifluoromethyl, trifluoromethoxy, carboxyl, halogen, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 4 carbon atoms, or represent straight-chain or branched alkoxy having up to 4 carbon atoms, or represent straight-chain or branched alkyl having up to 6 carbon atoms which is optionally mono- or polysubstituted by identical or different substituents from the group consisting of hydroxyl, fluorine, chlorine, bromine, phenyl, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 4 carbon atoms or by a group of the formula $-(CO)_d-NR^{14}R^{15}$,

in which

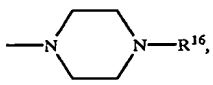
R^{14} and R^{15} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms,

and

d represents a number 0 or 1,

or

R^7 and R^8 and/or $R^{7'}$ and $R^{8'}$ together with the nitrogen atom form a pyrrolidinyl, piperidinyl or morpholinyl ring or a radical of the formula



in which

R^{16} represents hydrogen, phenyl, naphthyl or straight-chain or branched alkyl having up to 4 carbon atoms, which is optionally substituted by hydroxyl,

R^9 and $R^{9'}$ are identical or different and represent phenyl or benzyl, or represent straight-chain or branched alkyl having up to 3 carbon atoms,

R^{10} and R^{11} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms,

and/or the alkyl chain mentioned above under R^3/R^4 is optionally substituted by phenyl, naphthyl, morpholinyl, pyridyl, tetrahydropyranyl, tetrahydrofuranyl or thienyl, where the radical may optionally also be attached to the alkyl chain via a ring nitrogen atom,

and where aryl and the heterocycle are optionally mono- to disubstituted by identical or different substituents from the group consisting of nitro, fluorine, chlorine, bromine, $-SO_3H$, straight-chain or branched monohydroxy-substituted alkyl, alkylthio or alkoxy having in each case up to 4 carbon atoms, hydroxyl, trifluoromethyl, trifluoromethoxy and/or by a radical of the formula $-(SO_2)_e-NR^{18}R^{19}$,

in which

e represents a number 0 or 1,

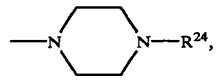
R^{18} and R^{19} are identical or different and represent hydrogen, phenyl, benzyl or straight-chain or branched alkyl or acyl having in each case up to 4 carbon atoms,

and/or

R^3 and R^4 represent radicals of the formulae $-NR^{20}R^{21}$ or $-(O)-E-NR^{22}R^{23}$,

in which

R^{20} and R^{21} have the meaning of R^{18} and R^{19} given above and are identical to or different from this meaning, or together with the nitrogen atom form a morpholinyl ring, pyrrolidinyl ring or a radical of the formula



in which

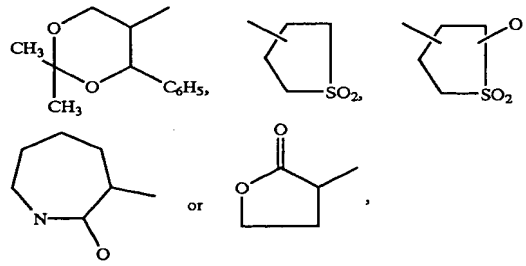
R^{24} has the meaning of R^{16} given above and is identical to or different from this meaning,

E represents a straight-chain alkylene group having up to 4 carbon atoms,

R^{22} and R^{23} have the meaning of R^{18} and R^{19} given above and are identical to or different from this meaning,

and/or

R^3 or R^4 represent radicals of the formulae

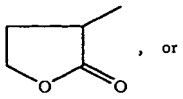


or represent cyclopentyl, cyclohexyl, naphthyl, phenyl pyridyl, or quinolyl or tetrazolyl attached via the phenyl ring,

and where the ring systems given above are optionally mono- to disubstituted by identical or different substituents from the group consisting of fluorine, chlorine, trifluoromethyl, trifluoromethoxy, carboxyl, straight-chain or branched acyl and alkoxycarbonyl having in each case up to 4 carbon atoms and/or by groups of the formulae $-SO_3H$, $-OR^{26}$, $(SO_2)_fNR^{27}R^{28}$, $-P(O)(OR^{29})(OR^{30})$,

in which

R^{26} represents a radical of the formula



represents cyclopentyl or cyclohexyl, or represents hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms which is optionally substituted by straight-chain or branched alkoxy or alkoxycarbonyl having in each case up to 4 carbon atoms, hydroxyl, carboxyl or phenyl, which for its part may be mono- to disubstituted by identical or different substituents from the group consisting of straight-chain or branched alkoxy having up to 3 carbon atoms, hydroxyl and halogen,

f represents a number 0 or 1,

R^{27} and R^{28} have the meaning of R^{18} and R^{19} given above and are identical to or different from this meaning or represent a radical of the formula $-CO-NH_2$,

R^{29} and R^{30} have the meaning of R^{10} and R^{11} given above and are identical to or different from this meaning,

and/or the ring systems given above are optionally substituted by straight-chain or branched alkyl having up to 4 carbon atoms, which are optionally substituted by hydroxyl, carboxyl, morpholine, pyridyl or by groups of the formula $-SO_2-R^{31}$, $P(O)(OR^{32})(OR^{33})$ or $-NR^{34}R^{35}$,

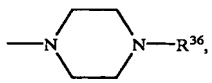
in which

R^{31} represents hydrogen or has the meaning of R^9 given above and is identical to or different from this meaning,

R^{32} and R^{33} have the meaning of R^{10} and R^{11} given above and are identical to or different from this meaning,

R^{34} and R^{35} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms which is optionally substituted by hydroxyl or straight-chain or branched alkoxy having up to 3 carbon atoms, or

R^{34} and R^{35} together with the nitrogen atom form a morpholinyl, pyrrolidinyl, piperidinyl ring or a radical of the formula

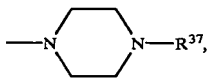


in which

R^{36} has the meaning of R^{16} given above and is identical to or different from this meaning,

or

R^3 and R^4 together with the nitrogen atom form a piperidinyl, pyrrolidinyl or morpholinyl ring, or a radical of the formula



in which

R^{37} represents hydrogen, hydroxyl, formyl, trifluoromethyl, straight-chain or branched acyl,

alkoxy or alkoxycarbonyl having in each case up to 4 carbon atoms, or represents cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl, or represents straight-chain or branched alkyl having up to 4 carbon atoms which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, trifluoromethyl, pyridyl, carboxyl, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 4 carbon atoms,

or

R^{37} represents a radical of the formula $—(CO)_g—G$, in which

g represents a number 0 or 1,

G represents naphthyl, phenyl, pyridyl or pyrimidyl, where the ring systems listed above are optionally mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, straight-chain or branched alkoxy, alkyl or alkylthio having in each case up to 4 carbon atoms, hydroxyl and trifluoromethyl,

and the heterocycles listed above under R^3 and R^4 are optionally mono- to trisubstituted, optionally also geminally, by identical or different substituents from the group consisting of hydroxyl, formyl, carboxyl, straight-chain or branched acyl or alkoxycarbonyl having in each case up to 4 carbon atoms and groups of the formulae $—P(O)(OR^{38})(OR^{39})$ or $—(CO)_g—NR^{40}R^{41}$, in which

R^{38} and R^{39} have the meaning of R^{10} and R^{11} given above and are identical to or different from this meaning,

g represents a number 0 or 1,

and

R^{40} and R^{41} are identical or different and have the meaning of R^{18} and R^{19} given above,

and/or the heterocycles listed under R^3 and R^4 are optionally substituted by straight-chain or branched alkyl having up to 4 carbon atoms which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, fluorine, chlorine, carboxyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclopentyloxy, cyclohexyloxy, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 4 carbon atoms or by a radical of the formula $—SO_3H$, $—NR^{42}R^{43}$ or $P(O)OR^{44}OR^{45}$, in which

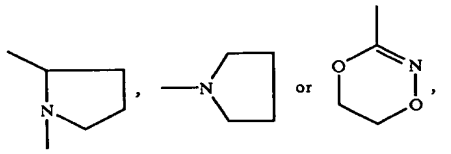
R^{42} and R^{43} are identical or different and represent hydrogen, phenyl, carboxyl, benzyl or straight-chain or branched alkyl or alkoxy having in each case up to 4 carbon atoms,

R^{44} and R^{45} are identical or different and have the meaning of R^{10} and R^{11} given above,

and/or the alkyl is optionally substituted by benzyloxy, naphtyl or phenyl, which for its part may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, hydroxyl, straight-chain or branched alkoxy and alkylthio having in each case up to 4 carbon atoms, or by a group of the formula $—NR^{42'}R^{43'}$, in which

$R^{42'}$ and $R^{43'}$ have the meaning of R^{42} and R^{43} given above and are identical to or different from this meaning,

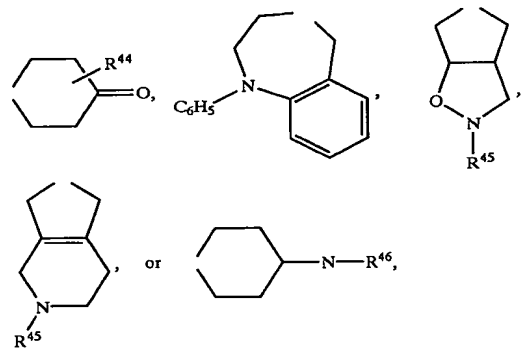
and/or the heterocycles listed under R^3 and R^4 are optionally substituted by phenyl, naphthyl or by radicals of the formulae



where the ring systems for their part may be substituted by fluorine, chlorine, hydroxyl or by straight-chain or branched alkyl, alkylthio or alkoxy having in each case up to 4 carbon atoms,

or

R^3 and R^4 together with the nitrogen atom form radicals of the formulae



in which

R^{44} represents hydrogen or straight-chain or branched alkyl or alkoxycarbonyl having in each case up to 3 carbon atoms,

R^{45} and $R^{45'}$ are identical or different and represent hydrogen or methyl,

R^{46} represents hydroxyl or straight-chain or branched alkoxy having up to 4 carbon atoms,

R^5 and R^6 are identical or different and represent hydrogen, straight-chain or branched alkyl having up to 4 carbon atoms, hydroxyl or represent straight-chain or branched alkoxy having up to 4 carbon atoms,

and their salts and isomeric forms.

Particular preference is given to compounds of the general formula (I) according to the invention,

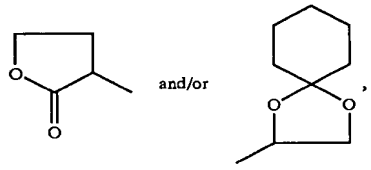
in which

R^1 represents straight-chain or branched alkyl having up to 3 carbon atoms,

R^2 represents straight-chain alkyl having 5 to 12 carbon atoms or branched alkyl having 3 to 12 carbon atoms, or represents cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl or cyclooctyl,

R^3 and R^4 are identical or different and represent hydrogen, or represent straight-chain or branched alkenyl having up to 4 carbon atoms, or represent a straight-chain or branched alkyl chain having up to 6 carbon atoms which is optionally interrupted by an oxygen atom and which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, carboxyl, straight-chain or branched alkoxy, alkoxycarbonyl and alkylthio having in each case up to 4 carbon atoms and/or by radicals

of the formulae $-SO_3H$, $-(A)_a-NR^7R^8$, $-O-CO-NR^{7'}R^{8'}$, $-S(O)_b-R^9$, $HN=SO-R^{9'}$, $-P(O)(OR^{10})(OR^{11})$,



in which

a and b are identical or different and represent a number 0 or 1,

A represents a radical CO or SO_2,

R^7, $R^{7'}$, R^8 and $R^{8'}$ are identical or different and represent hydrogen, or represent phenyl, naphthyl, or pyridyl, where the ring systems listed above are optionally mono- to disubstituted by identical or different substituents from the group consisting of hydroxyl, nitro, trifluoromethyl, trifluoromethoxy, carboxyl, halogen, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 4 carbon atoms, or represent straight-chain or branched alkoxy having up to 4 carbon atoms, or represent straight-chain or branched alkyl having up to 6 carbon atoms which is optionally mono- or polysubstituted by identical or different substituents from the group consisting of hydroxyl, fluorine, chlorine, bromine, phenyl, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 4 carbon atoms or by a group of the formula $-(CO)_d-NR^{14}R^{15}$,

in which

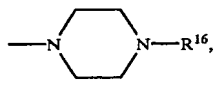
R^{14} and R^{15} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms,

and

d represents a number 0 or 1,

or

R^7 and R^8 and/or $R^{7'}$ and $R^{8'}$ together with the nitrogen atom form a pyrrolidinyl, piperidinyl or morpholinyl ring or a radical of the formula



in which

R^{16} represents hydrogen, phenyl, naphthyl or straight-chain or branched alkyl having up to 4 carbon atoms which is optionally substituted by hydroxyl,

R^9 and $R^{9'}$ are identical or different and represent phenyl or benzyl, or represent straight-chain or branched alkyl having up to 3 carbon atoms,

R^{10} and R^{11} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms,

and/or the alkyl chain listed above under R^3/R^4 is optionally substituted by phenyl, naphthyl, morpholinyl, pyridyl, tetrahydropyranyl, tetrahydrofuranyl or thienyl, where the attachment to the alkyl chain may optionally also take place via a ring nitrogen atom,

and where aryl and the heterocycle are optionally mono- to disubstituted by identical or different substituents from the group consisting of nitro, fluorine, chlorine, bromine, $-SO_3H$, straight-chain or branched monohydroxy-substituted alkyl, alkylthio or alkoxy having in each case up to 4 carbon atoms, hydroxyl, trifluoromethyl, trifluoromethoxy and/or by a radical of the formula $-(SO_2)_e-NR^{18}R^{19}$,

in which

e represents a number 0 or 1,

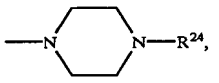
R^{18} and R^{19} are identical or different and represent hydrogen, phenyl, benzyl or straight-chain or branched alkyl or acyl having in each case up to 4 carbon atoms,

and/or

R^3 or R^4 represents radicals of the formulae $-NR^{20}R^{21}$ or $-(O)-E-NR^{22}R^{23}$,

in which

R^{20} and R^{21} have the meaning of R^{18} and R^{19} given above and are identical to or different from this meaning, or together with the nitrogen atom form a morpholinyl ring, pyrrolidinyl ring or a radical of the formula



in which

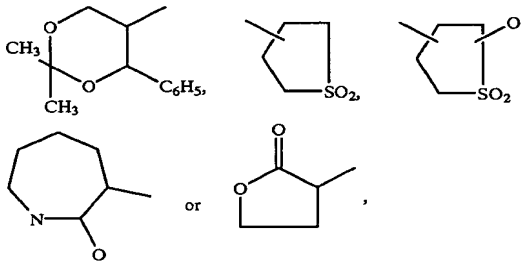
R^{24} has the meaning of R^{16} given above and is identical to or different from this meaning,

E represents a straight-chain alkylene group having up to 4 carbon atoms,

R^{22} and R^{23} have the meaning of R^{18} and R^{19} given above and are identical to or different from this meaning

and/or

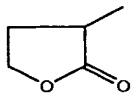
R^3 or R^4 represent the radicals of the formulae



or represent cyclopentyl, cyclohexyl, naphthyl, phenyl, pyridyl, or quinolinyl or tetrazolyl attached via the phenyl ring,

and where the ring systems given above are optionally mono- to disubstituted by identical or different substituents from the group consisting of fluorine, chlorine, trifluoromethyl, trifluoromethoxy, carboxyl, straight-chain or branched acyl and alkoxycarbonyl having in each case up to 4 carbon atoms and/or by groups of the formulae $-SO_3H$, $-OR^{26}$, $(SO_2)_fNR^{27}R^{28}$, $-P(O)(OR^{29})(OR^{30})$,

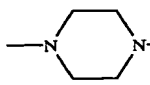
in which
R^{26} represents a radical of the formula



, or

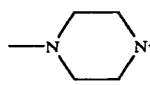
represents cyclopentyl or cyclohexyl, or represents hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms which is optionally substituted by straight-chain or branched alkoxy or alkoxycarbonyl having in each case up to 4 carbon atoms, hydroxyl, carboxyl or phenyl, which for its part may be mono- to disubstituted by identical or different substituents from the group consisting of straight-chain or branched alkoxy having up to 3 carbon atoms, hydroxyl and halogen,
f represents a number 0 or 1,
R^{27} and R^{28} have the meaning of R^{18} and R^{19} given above and are identical to or different from this meaning or represent a radical of the formula —CO—NH_2,
R^{29} and R^{30} have the meaning of R^{10} and R^{11} given above and are identical to or different from this meaning,

and/or the ring systems given above are optionally substituted by straight-chain or branched alkyl having up to 4 carbon atoms which are optionally substituted by hydroxyl, carboxyl, morpholine, pyridyl or by groups of the formula —SO_2—R^{31}, P(O)(OR^{32})(OR^{33}) or —$NR^{34}R^{35}$,
in which
R^{31} represents hydrogen or has the meaning of R^9 given above and is identical to or different from this meaning,
R^{32} and R^{33} have the meaning of R^{10} and R^{11} given above and are identical to or different from this meaning,
R^{34} and R^{35} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms which is optionally substituted by hydroxyl or straight-chain or branched alkoxy having up to 3 carbon atoms, or
R^{34} and R^{35} together with the nitrogen atom form a morpholinyl, pyrrolidinyl, piperidinyl ring or a radical of the formula



in which
R^{36} has the meaning of R^{16} given above and is identical to or different from this meaning,

or
R^3 and R^4 together with the nitrogen atom form a piperidinyl, pyrrolidinyl or morpholinyl ring, or a radical of the formula

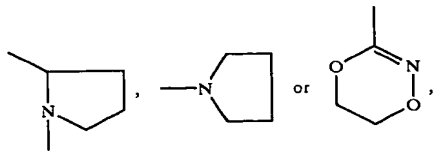


in which
R^{37} represents hydrogen, hydroxyl, formyl, trifluoromethyl, straight-chain or branched acyl, alkoxy or alkoxycarbonyl having in each case up to 4 carbon atoms, or represents cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl, or represents straight-chain or branched alkyl having up to 4 carbon atoms which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, trifluoromethyl, pyridyl, carboxyl, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 4 carbon atoms,
or
R^{37} represents a radical of the formula —$(CO)_g$—G,
in which
g represents a number 0 or 1,
G represents naphthyl, phenyl, pyridyl or pyrimidyl, where the ring systems listed above are optionally mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, straight-chain or branched alkoxy, alkyl or alkylthio having in each case up to 4 carbon atoms, hydroxyl and trifluoromethyl,

and the heterocycles listed under R^3 and R^4 are optionally mono- to trisubstituted, optionally also geminally, by identical or different substituents from the group consisting of hydroxyl, formyl, carboxyl, straight-chain or branched acyl or alkoxycarbonyl having in each case up to 4 carbon atoms and groups of the formulae —P(O)(OR^{38})(OR^{39}) or —$(CO)_g$—$NR^{40}R^{41}$,
in which
R^{38} and R^{39} have the meaning of R^{10} and R^{11} given above and are identical to or different from this meaning,
g represents a number 0 or 1,
and
R^{40} and R^{41} are identical or different and have the meaning of R^{18} and R^{19} given above,

and/or the heterocycles listed under R^3 and R^4 are optionally substituted by straight-chain or branched alkyl having up to 4 carbon atoms which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, fluorine, chlorine, carboxyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclopentyloxy, cyclohexyloxy, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 4 carbon atoms or by a radical of the formula —SO_3H, —$NR^{42}R^{43}$ or P(O)$OR^{44}OR^{45}$,
in which
R^{42} and R^{43} are identical or different and represent hydrogen, phenyl, carboxyl, benzyl or straight-chain or branched alkyl or alkoxy having in each case up to 4 carbon atoms,
R^{44} and R^{45} are identical or different and have the meaning of R^{10} and R^{11} given above,
and/or the alkyl is optionally substituted by benzyloxy, naphtyl or phenyl, which for its part may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, hydroxyl, straight-chain or branched alkoxy or alkylthio having in each case up to 4 carbon atoms, or by a group of the formula —$NR^{42'}R^{43'}$
in which
$R^{42'}$ and $R^{43'}$ have the meaning of R^{42} and R^{43} given above and are identical to or different from this meaning,

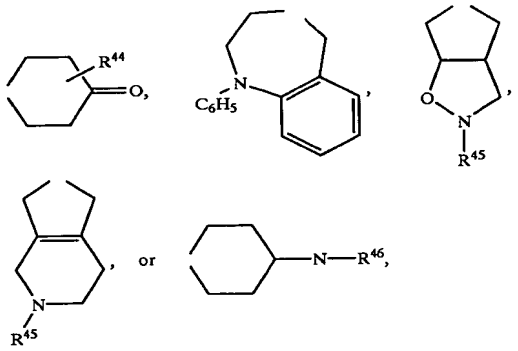
and/or the heterocycles listed under R^3 and R^4 are optionally substituted by phenyl, naphthyl or by radicals of the formulae



where the ring systems for their part may be substituted by fluorine, chlorine, hydroxyl or by straight-chain or branched alkyl, alkylthio or alkoxy having in each case up to 4 carbon atoms,

or

R^3 and R^4 together with the nitrogen atom form radicals of the formulae



in which

R^{44} represents hydrogen or straight-chain or branched alkyl or alkoxycarbonyl having in each case up to 3 carbon atoms,

R^{45} and $R^{45'}$ are identical or different and represent hydrogen or methyl,

R^{46} represents hydroxyl or straight-chain or branched alkoxy having up to 4 carbon atoms,

R^5 and R^6 are identical or different and represent hydrogen, straight-chain or branched alkyl having up to 4 carbon atoms, hydroxyl or represent straight-chain or branched alkoxy having up to 4 carbon atoms.

and their salts and isomeric forms.

Particular preference is also given to compounds of the general formula (I) in which

R^1 represents methyl or ethyl,

R^2 represents straight-chain alkyl having 5 to 11 carbon atoms or branched alkyl having 3 to 11 carbon atoms, or represents cyclopentyl, cyclohexyl, cycloheptyl,

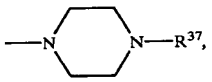
R^3 and R^4 are identical or different and represent straight-chain or branched alkyl having up to 4 carbon atoms which is optionally substituted by hydroxyl, morpholinyl, methoxy, ethoxy, N,N-dimethylamino, N,N-diethylamine or phenyl, which for its part may be substituted up to 3 times by identical or different substituents from the group consisting of methoxy, or represents cyclopropyl, or or represents phenyl which is optionally substituted up to 3 times by identical or different substituents from the group consisting of fluorine, chlorine or hydroxyl, methoxy, ethoxy, fluorine or by straight-chain or branched alkyl having up to 3 carbon atoms, which for its part may be substituted by hydroxyl,

or

R^3 and R^4 together with the nitrogen atom form a morpholinyl, pyrrolidinyl or piperidinyl ring which are optionally substituted by hydroxyl or by radicals of the formulae $-P(O)(OC_2H_5)_2$ or $-CH_2-P(O)OH(OC_2H_5)$ or by straight-chain or branched alkyl having up to 3 carbon atoms, which for its part may be substituted by hydroxyl or methoxy, or

or

R^3 and R^4 together with the nitrogen atom form a radical of the formula



in which

R^{37} represents pyrimidyl, ethoxycarbonyl or a radical of the formula $-CH_2-P(O)(OCH_3)_2$ or represents straight-chain or branched alkyl having up to 3 carbon atoms which is optionally substituted by hydroxyl or methoxy,

R^5 represents hydrogen,

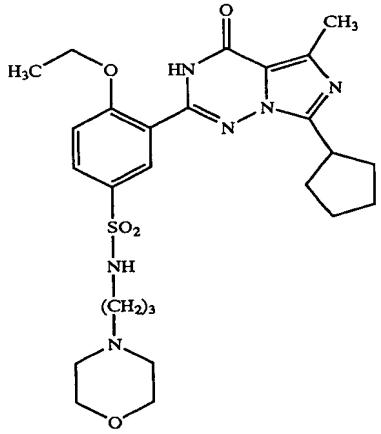
and

R^6 represents ethoxy,

and their salts and isomeric forms.

Particular preference is furthermore given to compounds of the general formula (I) according to the invention in which R^5 represents hydrogen and the ethoxy group is in the O position to the point of attachment of the heterocycle.

Very particular preference is given to compounds according to the invention having the following structures:

Structure


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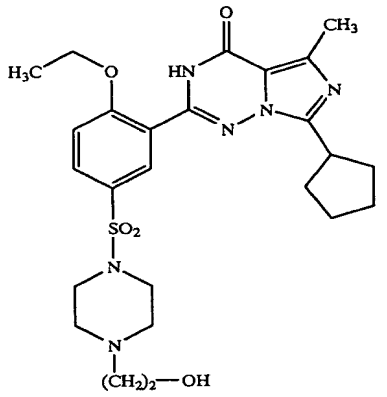
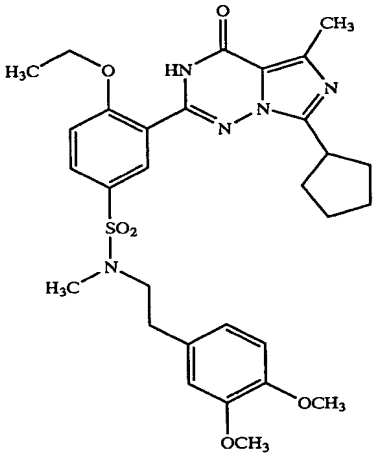
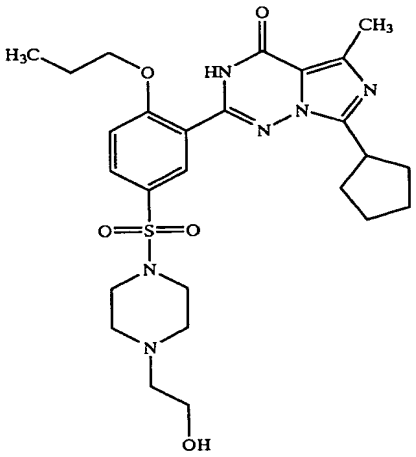
Structure




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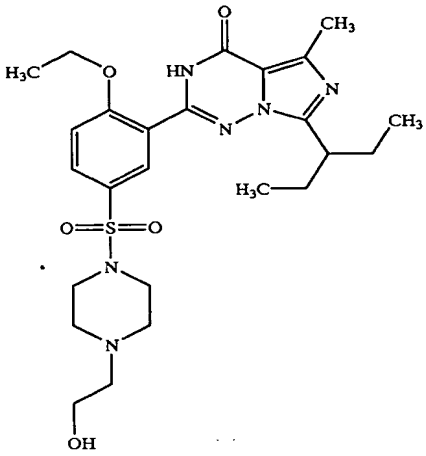
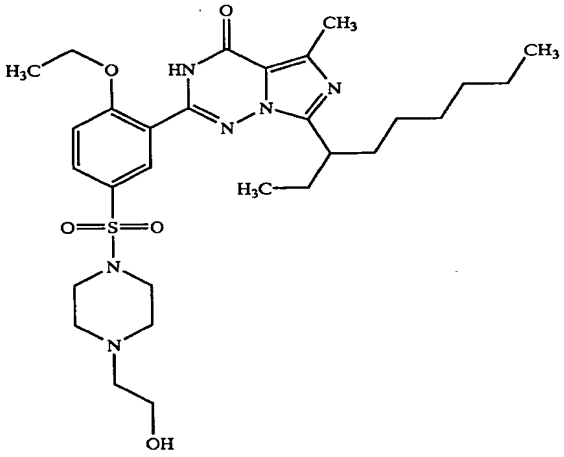
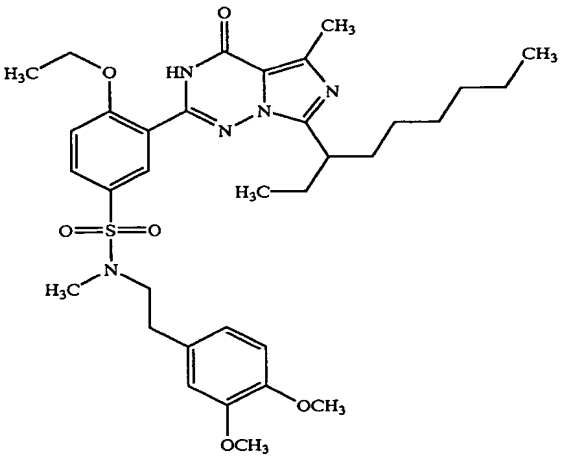
Structure




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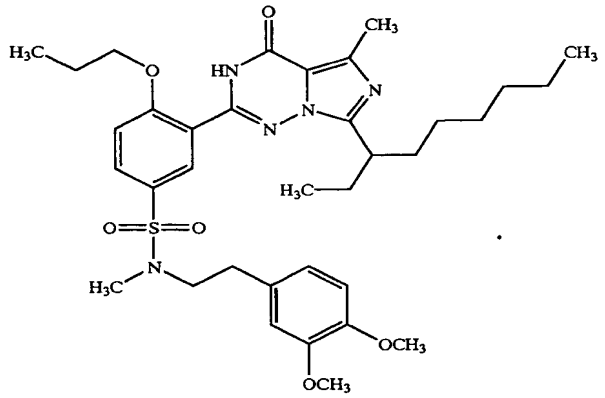
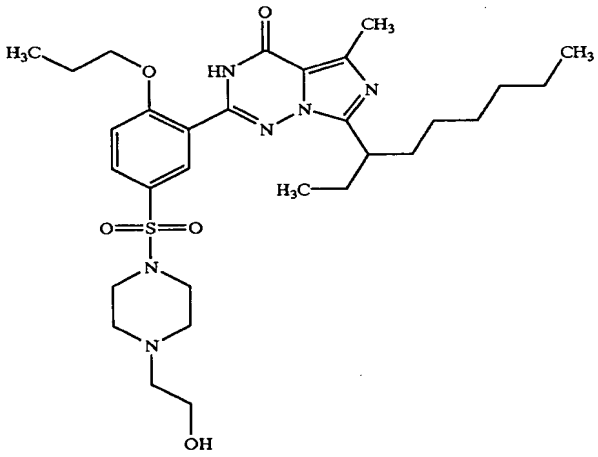
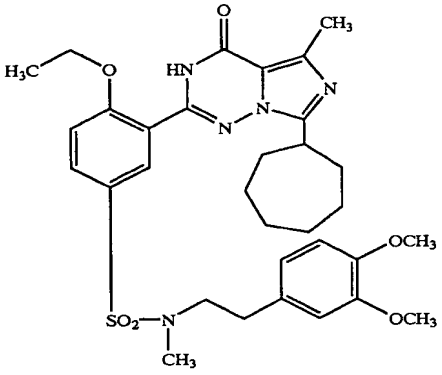

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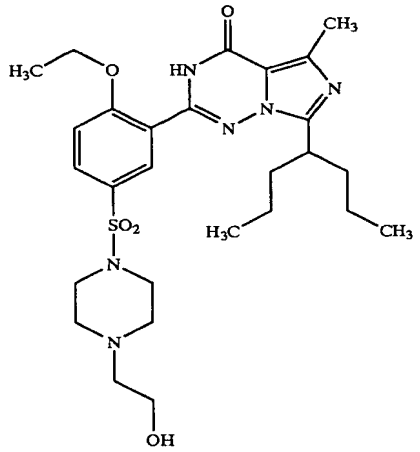
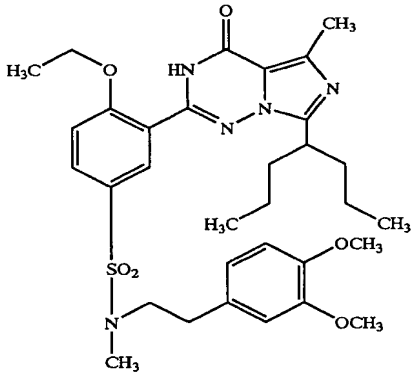
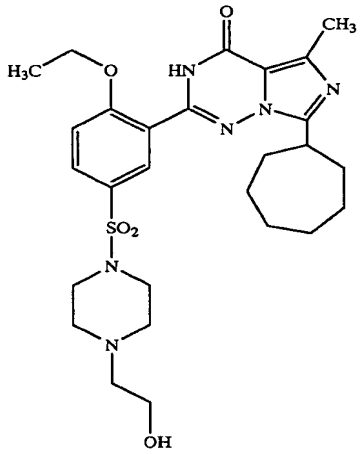

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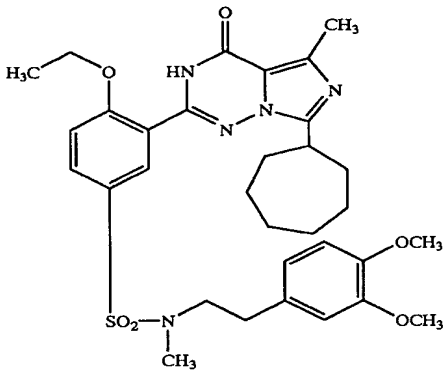
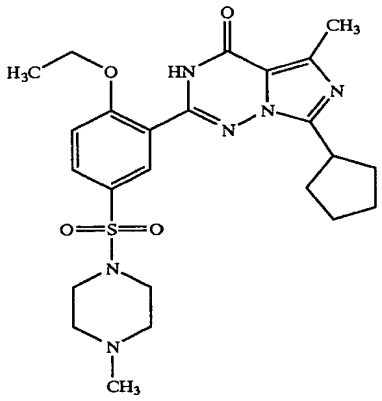
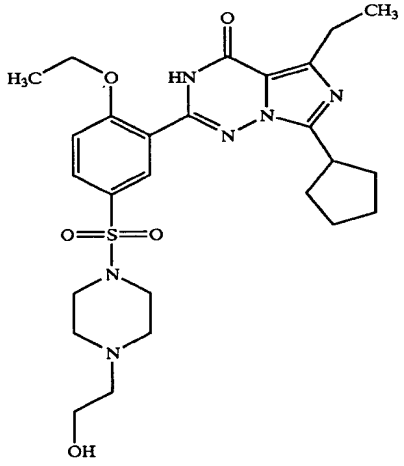
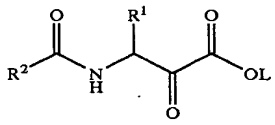
Structure




Moreover, we have found a process for preparing the compounds of the general formula (I) according to the invention, characterized in that

[A] initially compounds of the general formula (II)

(II)



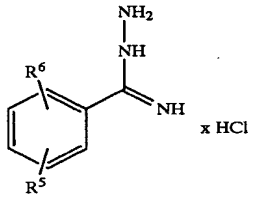
in which

R^1 and R^2 are as defined above

and

L represents straight-chain or branched alkyl having up to 4 carbon atoms, are converted with compounds of the general formula (III)

(III)

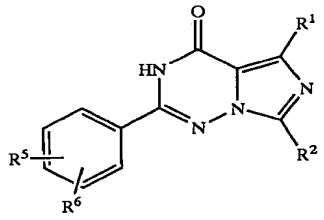


in which

R5 and R^6 are as defined above

in a two-step reaction, preferably using the system ethanol and then phosphorus oxytrichloride/dichloroethane, into the compounds of the general formula (IV)

(IV)

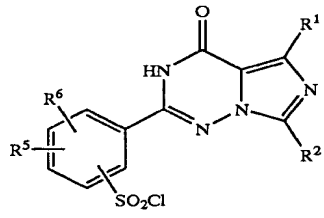


in which

R^1, R^2, R^5 and R^6 are as defined above,

in a further step reacted with chlorosulphonic acid to give the compounds of the general formula (V)

(V)



in which

R^1, R^2, R^5 and R^6 are as defined above,

and then reacted with amines of the general formula (VI)

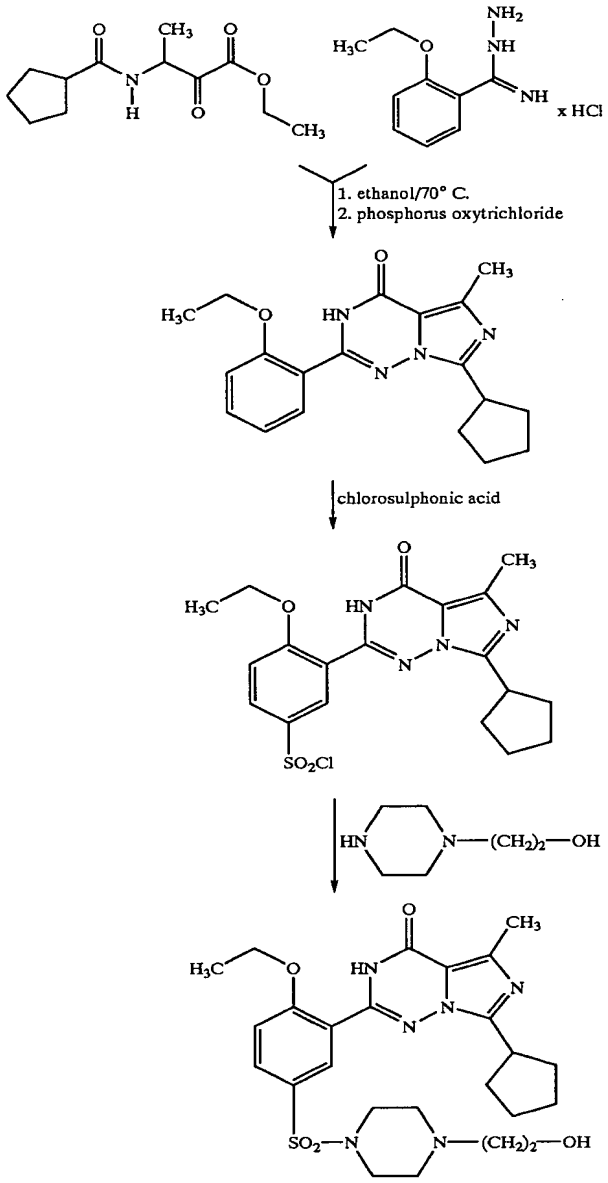
HN^3R^4 (VI)

in which

R^3 and R^4 are as defined above

in inert solvents.

The process according to the invention can be illustrated in an exemplary manner by the equations below:



Solvents which are suitable for the individual steps are the customary organic solvents which do not change under the reaction conditions. These preferably include ethers, such as diethyl ether, dioxane, tetrahydrofuran, glycol dimethyl ether, or hydrocarbons, such as benzene, toluene, xylene, hexane, cyclohexane or mineral oil fractions, or halogenated hydrocarbons, such as dichloromethane, trichloromethane, carbon tetrachloride, dichloroethane, trichloroethylene or chlorobenzene, or ethyl acetate, dimethylformamide, hexamethylphosphoric triamide, acetonitrile, acetone, dimethoxyethane or pyridine. It is also possible to use mixtures of the abovementioned solvents. Particular preference is given to ethanol for the first step and dichloroethane for the second step.

The reaction temperature can generally be varied within a relatively wide range. In general, the reaction is carried out in a range of from −20° C. to 200° C., preferably of from 0° C. to 70° C.

The process steps according to the invention are generally carried out under atmospheric pressure. However, it is also possible to operate under superatmospheric pressure or under reduced pressure (for example, in a range of from 0.5 to 5 bar).

The reaction to give the compounds of the general formula (V) is carried out in a temperature range of from 0° C. to room temperature, and at atmospheric pressure.

The reaction with the amines of the general formula (VI) is carried out in one of the abovementioned chlorinated hydrocarbons, preferably in dichloromethane.

The reaction temperature can generally be varied within a relatively wide range. In general, the reaction is carried out at temperatures in a range of from −20° C. to 200° C., preferably of from 0° C. to room temperature.

The reaction is generally carried out at atmospheric pressure. However, it is also possible to operate under superatmospheric pressure or under reduced pressure (for example in a range of from 0.5 to 5 bar).

Some of the compounds of the general formula (II) are known, or they are novel, and they can then be prepared by converting compounds of the general formula (VII)

(VII)

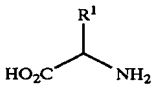
in which

R^2 is as defined above

and

T represents halogen, preferably represents chlorine, initially by reaction with compounds of the general formula (VIII)

(VIII)

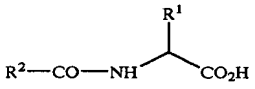


in which

R^1 is as defined above

in inert solvents, if appropriate in the presence of a base and trimethylsilyl chloride, into the compounds of the general formula (IX)

(IX)

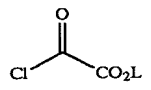


in which

R^1 and R^2 are each as defined above,

and finally reacting with the compound of the formula (X)

(X)



in inert solvents, if appropriate in the presence of a base.

Suitable solvents for the individual steps of the process are the customary organic solvents which do not change under the reaction conditions. These preferably include ethers, such as diethyl ether, dioxane, tetrahydrofuran, glycol dimethyl ether, or hydrocarbons, such as benzene, toluene, xylene, hexane, cyclohexane or mineral oil fractions, or halogenated hydrocarbons, such as dichloromethane, trichloromethane, carbon tetrachloride, dichloroethylene, trichloroethylene or chlorobenzene, or ethyl acetate, dimethylformamide, hexamethylphosphoric triamide, acetonitrile, acetone, dimethoxyethane or pyridine. It is also possible to use mixtures of the abovementioned solvents. Particular preference is given to dichloromethane for the first step and to a mixture of tetrahydrofuran and pyridine for the second step.

Suitable bases are generally alkali metal hydrides or alkali metal alkoxides, such as, for example, sodium hydride or potassium tert-butoxide, or cyclic amines, such as, for example, piperidine, pyridine, dimethylaminopyridine or C_1–C_4 alkylamines, such as, for example, triethylamine. Preference is given to triethylamine, pyridine and/or dimethylaminopyridine.

The base is generally employed in an amount of from 1 mol to 4 mol, preferably from 1.2 mol to 3 mol, in each case based on 1 mol of the compound of the formula (X).

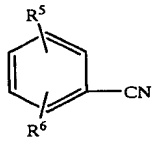
The reaction temperature can generally be varied within a relatively wide range. In general, the reaction is carried out in a range of from −20° C. to 200° C., preferably of from 0° C. to 100° C.

The compounds of the general formulae (VII), (VIII), (IX) and (X) are known per se, or they can be prepared by customary methods.

The compounds of the general formula (III) can be prepared by

reacting compounds of the general formula (XI)

(XI)



in which

R^5 and R^6 are each as defined above

with ammonium chloride in toluene and in the presence of trimethylaluminium in hexane in a temperature range of from −20° C. to room temperature, preferably at 0° C. and atmospheric pressure, and reacting the resulting amidine, if appropriate in situ, with hydrazine hydrate, to give the compounds of the general formula (III).

The compounds of the general formula (XI) are known per se, or they can be prepared by customary methods.

Most of the compounds of the general formula (IV) and (V) are novel, and they can be prepared as described above.

The amines of the general formula (VI) are known or can be prepared by customary methods.

The compounds of the general formula (I) according to the invention have an unforeseeable useful pharmacological activity spectrum.

They inhibit either one or more of the cGMP-metabolizing phosphodiesterases (PDE I, PDE II and PDE V). This results in an increase of cGMP. The differentiated expression of the phosphodiesterases in different cells, tissues and organs, as well as the differentiated subcellular localization of these enzymes, in combination with the selective inhibitors according to the invention make it possible to selectively address the various cGMP-regulated processes.

Moreover, the compounds according to the invention enhance the activity of substances such as, for example EDRF (endothelium derived relaxing factor), ANP (atrial natriuretic peptide), of nitrovasodilators and all other substances which increase the cGMP concentration in a manner different from that of phosphodiesterase inhibitors.

They can therefore be employed in pharmaceuticals for treating cardiovascular disorders, such as, for example, for treating hypertension, neuronal hypertonia, stable and unstable angina, peripheral and cardial vasculopathies, arrhythmiae, for treating thromboembolic disorders and ischaemias such as myocardial infarction, stroke, transistory and ischaemic attacks, angina pectoris, obstruction of peripheral circulation, prevention of restenoses after thrombolysis therapy, percutaneous transluminal angioplasty (PTA), percutaneous transluminal coronary angioplasties (PTCA) and bypass. Furthermore, they may also be of significance for cerebrovascular disorders.

They are also suitable for treating all disorders in which a relaxing action on smooth muscles is of importance, such as, for example, erectile dysfunction and female sexual dysfunction.

Activity of the Phosphodiesterases (PDEs)

The cGMP-stimulated PDE II, the cGMP-inhibited PDE III and the cAMP-specific PDE IV were isolated either from porcine or bovine heart myocardium. The Ca^{2+}- calmodulin-stimulated PDE I was isolated from porcine aorta, porcine brain or, preferably, from bovine aorta. The cGMP-specific PDE V was obtained from porcine small intestine, porcine aorta, human platelets and, preferably, from bovine aorta. Purification was carried out by anion exchange chromatography over MonoQ® Pharmacia, essentially following the method of M. Hoey and Miles D. Houslay, Biochemical Pharmacology, Vol. 40, 193–202 (1990) and C. Lugman et al., Biochemical Pharmacology, Vol. 35, 1743–1751 (1986).

The "phosphodiesterase [^{3}H] cAMP-SPA enzyme assay" and the "phosphodiesterase [^{3}H] cGMP-SPA enzyme assay" from Amersham Life Science were used for determining enzyme activity and IC_{50} values of the various substances. The test was carried out according to the test protocol of the manufacturer. To determine the activity of PDE2, the [^{3}H] cAMP SPA assay was used, and 10^{-6} M cGMP were added to the reaction mixture to activate the enzyme. To measure PDEI, 10^{-7} M calmodulin and 1 mM $CaCl_2$, were added to the reaction mixture. PDE5 was measured using the [^{3}H] cGMP SPA assay.

The substances preferably inhibit phosphodiesterases I and V. For both enzymes, the IC_{50} values are in the range from 500 to 1 mM for PDE V preferably in the range from 1 to 100 for PDE I preferably in the range from 10 to 300 mM.

In principle, inhibition of one or more phosphodiesterases of this type results in an increase of the cGMP concentration.

Thus, the compounds are of interest for all therapies in which an increase in the cGMP concentration is considered to be beneficial.

The cardiovascular effects were investigated using SH rats and dogs. The substances were administered intravenously or orally.

The novel active compounds and their physiologically acceptable salts (for example hydrochlorides, maleates or lactates) can be converted in a known manner into the customary formulations, such as tablets, coated tablets, pills, granules, aerosols, syrups, emulsions, suspensions and solutions, using inert non-toxic, pharmaceutically suitable excipients or solvents. In this case the therapeutically active compound should in each case be present in a concentration of from approximately 0.5 to 90% by weight of the total mixture, i.e. in amounts which are sufficient in order to achieve the dosage range indicated.

The formulations are prepared, for example, by extending the active compounds using solvents and/or excipients, if appropriate using emulsifiers and/or dispersants, it optionally being possible, for example, to use organic solvents as auxiliary solvents if the diluent used is water.

Administration is carried out in a customary manner, preferably orally, transdermally or parenterally, for example perlingually, buccally, intravenously, nasally, rectally or inhalatively.

In spite of this, if appropriate it may be necessary to depart from the amounts mentioned, namely depending on the body weight or the type of administration route, on the individual response towards the medicament, the manner of its formulation and the time or interval at which administration takes place. Thus, in some cases it may be adequate to manage with less than the abovementioned minimum amounts, while in other cases the upper limit mentioned has to be exceeded. In the case of the administration of relatively large amounts, it may be advisable to divide these into several individual doses over the course of the day.

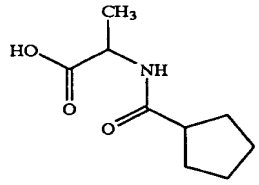
For human use, in the case of oral administration, doses of from 0.001 to 30 mg/kg, preferably of 0.01 mg/kg–10 mg/kg are administered. In the case of parenteral administration, it is good practice to use doses of 0.001 mg/kg–½ mg/kg.

The compounds according to the invention are also suitable for use in veterinary medicine. For use in veterinary medicine, the compounds or their non-toxic salts can be administered in a suitable formulation in accordance with general veterinary practice. Depending on the kind of animal to be treated, the veterinary surgeon can determine the nature of use and the dosage.

STARTING MATERIALS

EXAMPLE 1A

2-Cyclopentanoylamino-propionic acid



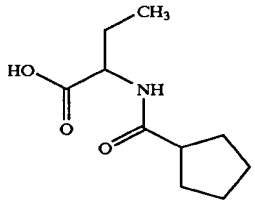
16.8 g (0.189 mol) of D,L-alanine and 41.98 g (0.415 mol) of triethylamine are initially charged in 200 ml of dichloromethane. At 0° C. 45.07 g (0.415 mol) of trimethylsilyl chloride are added dropwise, and the mixture is then stirred at room temperature for 1 h and then at 40° C. for 1 h. The solution is cooled to −10° C. and 25 g (0.189 mol) of cyclopentanecarbonyl chloride are added dropwise. The mixture is stirred at −10° C. for 2 h and at room temperature for 1 h. With ice-cooling, 100 ml of water are added, and the mixture is then stirred for 10 min and the resulting precipitate is filtered off with suction. The precipitate is washed with 300 ml of water and then with 300 ml of diethyl ether and subsequently dried at 60° C.

Yield: 25.8 g (73.9% of theory)

^{1}H-NMR (CD_3OD): 1.35 (d, 3H); 1.5–1.9 (m, 8H); 2.7 (quin, 1H); 4.5 (quar., 1H):

EXAMPLE 2A

2-Cyclopentanoylamino-butyric acid



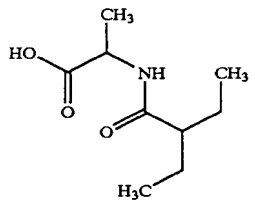
10.31 g of 2-aminobutyric acid (100 mmol) and 22.26 g (220 mmol) of triethylamine are dissolved in 100 ml of dichloromethane, and the solution is cooled to 0° C. 23.90 g (220 mmol) of trimethylsilyl chloride are added dropwise, and the solution is stirred at room temperature for 1 hour and at 40° C. for 1 hour. After cooling to −10° C., 13.26 g (100 mmol) of cyclopentanecarbonyl chloride are added dropwise, and the resulting mixture is stirred at −10° C. for 2 hours and at room temperature for 1 hour.

With ice-cooling, 50 ml of water are added dropwise and the reaction mixture is stirred at room temperature for 15 minutes. The mixture is diluted with water and dichloromethane and the resulting precipitate is filtered off with suction: 11.1 g (55%) of a colourless solid. The dichloromethane phase is dried over sodium sulphate and the solvent is removed under reduced pressure. The residue is stirred with toluene and the precipitate is filtered off with suction: 5.75 g (28%) of a colourless solid:

200 MHz ^{1}H-NMR (DMSO-d_6): 0.88 (t, 3H); 1.61 (m, 10H); 2.66 (m, 1H); 4.09 (hex., 1H); 7.97 (d, 1H); 12.44 (s, 1H).

EXAMPLE 3A

2-(2-Ethyl)-butanoylaminopropionic acid



24.5 g (0.275 mol) of D,L-alanine are initially charge in 250 ml of dichloromethane, and 61.2 g (0.605 mol) of

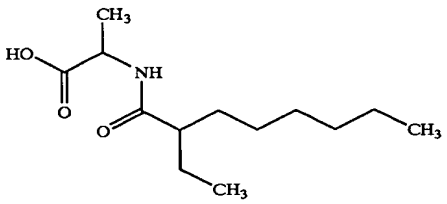
triethylamine are added. The mixture is cooled to 0° C. and 65.7 g (0.605 mol) of trimethylsilyl chloride are added. The mixture is stirred at room temperature for 1 hour and at 40° C. for 1 hour. The mixture is cooled to −10° C. and 37 g (0.275 mol) of 2-ethylbutyryl chloride are added dropwise. The mixture is stirred at −10° C. for 2 hours and at room temperature overnight. The mixture is cooled in an ice-bath and 150 ml of water are added dropwise. 50 g (1.25 mol) of NaOH dissolved in 100 ml of water, are added, and the aqueous phase is separated off and concentrated. The residue is again taken up in water and acidified with concentrated hydrochloric acid, the aqueous solution is extracted repeatedly with dichloromethane and the organic phase is dried over Na_2SO_4 and concentrated.

Yield: 43.55 g (84.6% of theory)

200 MHz ^{1}H-NMR ($CDCl_3$): 0.91 (t, 6H); 1.5 (d, 3H); 1.52–1.73 (m, 4H); 1.99 (m, 1H); 4.61 (p, 1H); 6.25 (d, 1H); 6.76 (bs, 1H).

EXAMPLE 4A

2-(2-Ethyl)-octanoylamino-propionic acid



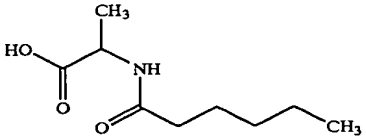
18.6 g (0.211 mol) of D,L-alanine and 46.6 g (0.41 mol) of triethylamine are initially charged in 300 ml of dichloromethane. at 0° C., 50.09 g (0.461 mol) of trimethylsilyl chloride are added dropwise, and the mixture is stirred at room temperature for 1 h and then at 40° C. for 1 h. The solution is cooled to −10° C., and 40 g (0.21 mol) of 2-ethyloctanoyl chloride in 50 ml of dichloromethane are added dropwise. The mixture is stirred at room temperature overnight, and 100 ml of water are then added dropwise with ice-cooling, and the mixture is stirred for another 10 minutes. The phases are separated, the aqueous phase is extracted twice with in each case 100 ml of dichloromethane and the combined organic phases are dried over sodium sulphate and evaporated under reduced pressure. The residue is recrystallized from toluene by adding n-hexane and dried at 60° C.

Yield: 3.9 g (78.2%)

^{1}H-NMR ($CDCl_3$): 0.9 (m, 6 h); 1.25 (pseudo s, 8H); 1.45 (d, 3H); 1.4–1.7 (m, 4H); 2.0 (m, 1H); 4.6 (quin. 1H); 6.1 (d, 1H).

EXAMPLE 5A

2-Hexanoylamino-propionic acid



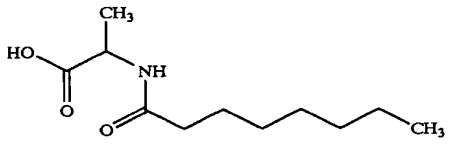
The preparation is carried out analogously to the procedure of Example 4A using 16.5 g (0.185 mol) of D,L-alanine, 41.23 g (0.407 mol) of triethylamine, 44.27 g (0.407 mol) of trimethylsilyl chloride and 24.93 g (0.185 mol) of hexanoyl chloride. The product crystallizes from toluene/n-hexane.

Yield: 33 g (95.2%)

^{1}H-NMR (CD_3OD): 0.9 (t, 3H); 1.2–1.4 (m, 7H); 1.6 (quin, 2H); 2.2 (t, 2H); 4.35 (quin, 1H).

EXAMPLE 6A

2-Octanoylamino-propionic acid



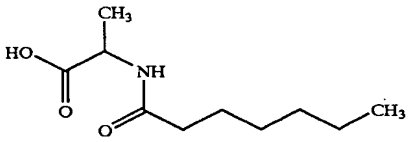
The preparation is carried out analogously to the procedure of Example 4A using 16.5 g (0.185 mol) of D,L-alanine, 41.23 g (0.407 mol) of triethylamine, 44.27 g (0.407 mol) of trimethylsilyl chloride and 30.12 g (0.185 mol) of octanoyl chloride. The product crystallizes from toluene/n-hexane.

Yield: 34.3 g (86%)

^{1}H-NMR (CD_3OD): 0.9 (t, 3H); 1.2–1.4 (m, 11H); 1.6 (quin. 2H); 2.2 (t, 2H); 4.35 (quin. 1H).

EXAMPLE 7A

2-Heptanoylamino-propionic acid



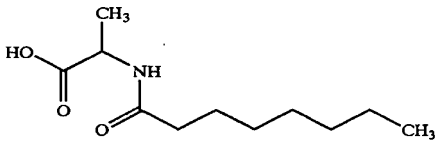
30 g (291 mmol) of methyl D,L-alaninate hydrochloride and 64.77 g (640 mmol) of triethylamine are initially charged in 300 ml of dry methylene chloride, at 0° C. 43.24 g (291 mmol) of heptanoyl chloride in 50 ml of methylene chloride are added dropwise. The mixture is allowed to warm to room temperature and stirred at this temperature for 2 h. The precipitate is filtered off, and the methylene chloride phase is extracted with saturated sodium bicarbonate solution and with saturated sodium chloride solution and dried over sodium sulphate. The solvent is removed under reduced pressure and the residue is dissolved in 300 ml of methanol. 300 ml of water, in which 46.55 g (1164 mmol) of sodium hydroxide are dissolved, is added to this solution, and the mixture is stirred at RT for 2 h. The mixture is filtered, the methanol is removed using a rotary evaporator and the aqueous phase that remains is acidified with conc. Hcl to pH 1–2. The precipitated product is filtered off and dried. A second product fraction is obtained by extracting the aqueous phase with ethyl acetate.

Yield: 50 g (85.4%)

^{1}H-NMR (CD_3OD): 0.9 (t, 3H); 1.2–1.4 (m, 9H); 1.6 (quin., 2H); 2.2 (t, 2H); 4.38 (quar., 1H).

EXAMPLE 8A

2-Decanoylamino-propionic acid



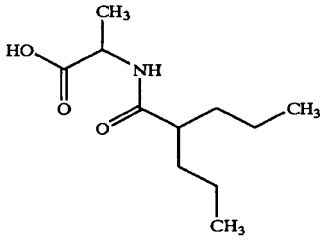
The preparation is carried out analogously to the procedure of Example 7A using 19.0 g (184 mmol) of methyl D,L-alaninate hydrochloride and 35.14 g (184 mmol) of decanoyl chloride.

Yield: 3 7.34 g (83.2%)

^{1}H-NMR (CD_3OD): 0.9 (t, 3H); 1.2–1.4 (m, 15H); 1.6 (m, 2H); 2.2 (t, 2H); 4.35 (quar., 1H).

EXAMPLE 9A

2-(2-n-Propyl)-pentanoylamino-propionic acid



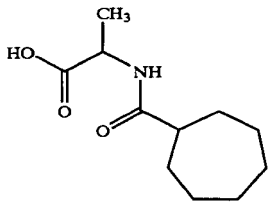
The preparation is carried out analogously to the procedure of Example 7A using 20.94 g (150 mmol) of methyl D,L-alaninate hydrochloride and 24.4 g (150 mmol) of 2-n-propylpentanoyl chloride.

Yield: 21.7 g (88.9%)

^{1}H-NMR (CD_3OD): 0.9 (t, 6H); 1.2–1.4 (m, 9H); 1.55 (m, 2H); 2.25 (m, 1H); 4.4 (quar., 1H).

EXAMPLE 10A

2-Cycloheptanoylamino-propionic acid



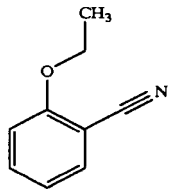
The preparation is carried out analogously to the procedure of Example 7A using 20 g (143 mmol) of methyl D,L-alaninate hydrochloride and 23.02 g (143 mmol) of cycloheptanoyl chloride.

Yield: 16 g (52.4%)

^{1}H-NMR (CD_3OD): 1.35 (d, 3H); 1.45–1.65 (m, 8H); 1.7–1.95 (m, 4H); 2.35 (m, 1H); 4.25 (quar., 1H).

EXAMPLE 11A

2-Ethoxy-benzonitrile

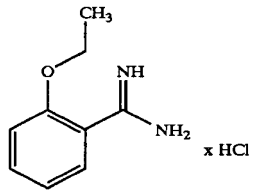


25 g (210 mmol) of 2-hydroxybenzonitrile, 87 g of potassium carbonate and 34.3 g (314.8 mmol) of ethyl bromide in 500 ml of acetone are refluxed overnight. The solid is filtered off, the solvent is removed under reduced pressure and the residue is distilled under reduced pressure. This gives 30.0 g (97%) of a colourless liquid.

200 MHz ^{1}H-NMR (DMSO-d_6): 1.48 (t, 3H); 4.15 (quart., 2H); 6.99 (dt, 2H); 7.51 (dt, 2H).

EXAMPLE 12A

2-Ethoxy-benzamidine hydrochloride

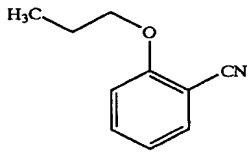


21.4 g (400 mmol) of ammonium chloride are suspended in 375 ml of toluene, and the suspension is cooled to 0° C. 200 ml of a 2M solution of trimethylaluminium in hexane are added dropwise, and the mixture is stirred at room temperature until evolution of gas has ceased. 29.44 g (200 mmol) of 2-ethoxybenzonitrile are added, and the reaction mixture is then stirred at 80° C. (bath) overnight. The cooled reaction mixture is, with ice-cooling, added to a suspension of 100 g of silica gel and 950 ml of chloroform, and the mixture is stirred at room temperature for 30 minutes. The mixture is filtered off with suction and the filter residue is washed with the same amount of methanol. The mother liquor is evaporated, the resulting residue is stirred with a mixture of dichloromethane and methanol (9:1), the solid is filtered off with suction and the mother liquor is evaporated. This gives 30.4 g (76%) of a colourless solid.

200 MHz ^{1}H-NMR (DMSO-d_6): 1.36 (t, 3H); 4.12 (quart., 2H); 7.10 (t, 1H); 7.21 (d, 1H); 7.52 (m, 2H); 9.30 (s, broad, 4H).

EXAMPLE 13A

2-Propoxybenzonitrile

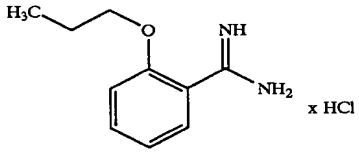


75 g (630 mmol) of 2-hydroxybenzonitrile, 174 g (1.26 mol) of potassium carbonate and 232.3 g (1.89 mol) of n-propyl bromide in 1 l of acetone are refluxed overnight. The solid is filtered off, the solvent is removed under reduced pressure and the residue is distilled under reduced pressure. B.p.: 89° C. (0.7 mbar)

Yield: 95.1 g (93.7% of theory)

EXAMPLE 14A

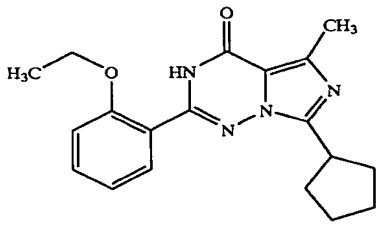
2-Propoxybenzamidine hydrochloride



21.41 g (400 ml) of ammonium chloride are suspended in 400 ml of toluene and cooled to from 0 to 5° C. 200 ml of a 2M solution of triethylaluminium in hexane are added dropwise, and the mixture is stirred at room temperature until evolution of gas has ceased. 32.2 g (200 mmol) of 2-propoxybenzonitrile are added, and the reaction mixture is then stirred at 80° C. (bath) overnight. The cooled reaction mixture is, with ice-cooling, added to a suspension of 300 g of silica gel and 2.85 ml of ice-cold chloroform and stirred for 30 minutes. The mixture is filtered off with suction and the filter residue is washed with the same amount of methanol. The solvent is distilled off under reduced pressure, the residue is stirred with 500 ml of a mixture of dichloromethane and methanol (9:1), the solid is filtered off and the mother liquor is evaporated. The residue is stirred with petroleum ether and filtered off with suction. This gives 22.3 g (52%) of product. 200 MHz ^{1}H-NMR (CD_3OD): 1.05 (t, 3H); 1.85 (sex, 2H); 4.1 (t, 2H); 7.0–7.2 (m, 2H); 7.5–7.65 (m, 2H).

EXAMPLE 15A

2-(2-Ethoxyphenyl)-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



19.9 g (0.1 mol) of 2-cyclopentanoylamino-propionic acid (Example 1A), 24 ml of pyridine and 0.5 g of 4-dimethylaminopyridine are refluxed in 100 ml of absolute tetrahydrofuran, and 27.27 g (0.2 mol) of ethyl oxalyl chloride are added dropwise. The mixture is boiled at reflux for 90 minutes, cooled and put into 200 ml of ice-water. The mixture is extracted 3 times with ethyl acetate and the combined ethyl acetate phases are dried over sodium sulphate and evaporated. The residue is taken up in 30 ml of methanol and, after addition of 4.75 g of sodium bicarbonate, refluxed for 2.5 h. The mixture is filtered off and the resulting methanolic solution of the α-keto ester is directly reacted further, without further purification.

With ice-cooling, 4.99 g (0.1 mol) of hydrazine monohydrate are added dropwise to a solution of 20 g (0.1 mol) of 2-ethoxy-benzamidine hydrochloride (Example 12A) in 120 ml of ethanol, and the mixture is stirred at room temperature for 10 minutes. The methanolic solution of the α-keto ester described above is added dropwise to the suspension, and the mixture is stirred at 70° C. for 4 h. Following filtration, the solution is evaporated, the residue is partitioned between dichloromethane and water and the organic phase is, after drying over sodium sulphate, evaporated.

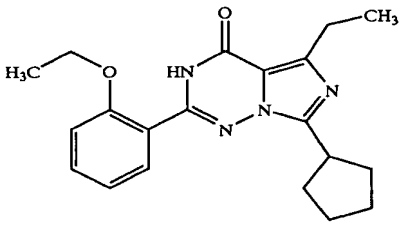
The residue is taken up in 150 ml of 1,2-dichloroethane, and 17 ml of phosphorus oxychloride are added dropwise. The mixture is stirred under reflux for 2 h and then cooled, washed twice with saturated sodium bicarbonate solution and dried over sodium sulphate. The organic phase is evaporated and the residue is chromatographed over silica gel using the mobile phase dichloromethane/methanol 50:1. The product-containing fractions are combined and evaporated. The product can be crystallized from ethyl acetate/petroleum ether.

Yield: 7.1 g (20.9%), white solid

^{1}H-NMR (CD_3OD): 1.45 (t, 3H); 1.65–1.8 (m, 2H); 1.8–2.0 (m, 4H); 2.05–2.2 (m, 2H); 2.6 (s, 3H); 3.65 (quin., 1H); 4.2 (quar, 2H); 7.1 (t, 1H); 7.15 (d, 1H); 7.5 (t, 1H); 7.7 (d, 1H).

EXAMPLE 16A

2-(2-Ethoxyphenyl)-5-ethyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one



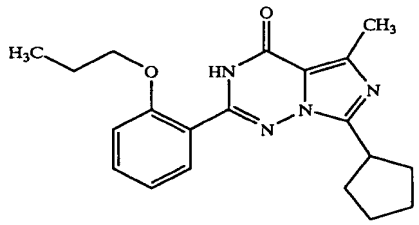
The preparation is carried out analogously to the procedure of Example 15A using 8.77 g (44 mmol) of 2-cyclopentanoylamino-butyric acid (Example 2A) and 8.83 g (44 mmol) of 2-ethoxy-benzamidine hydrochloride (Example 12A). The product is purified by silica gel chromatography using the mobile phase cyclohexane/ethyl acetate (6:4).

Yield: 0.355 g (6.7%), white solid

^{1}H-NMR ($CDCl_3$): 1.32 (t, 3H); 1.57 (t, 3H); 1.94 (m, 8H); 3.03 (quar, 2H); 3.64 (quin, 1H); 4.27 (quar, 2H), 7.06 8d, 1H); 7.12 (t, 1H); 7.50 (t, 1H); 8.16 (dd, 1H); 9.91 (s, 1H).

EXAMPLE 17A

2-(2-Propoxyphenyl)-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one



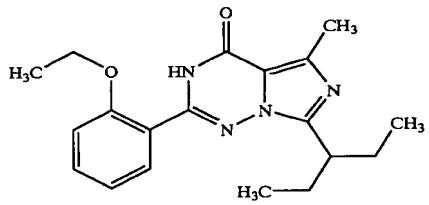
The preparation is carried out analogously to the procedure of Example 15A using 8.33 g (45 mmol) of 2-cyclopentanoylamino-propionic acid (Example 1A) and 9.65 g (45 mmol) of 2-propoxybenzamidine hydrochloride (Example 14A). The product is purified by silica gel chromatography using the mobile phase dichloromethane/methanol (50:1). The product can be crystallized from ethyl acetate/petroleum ether.

Yield: 1.82 g (11.5%), white solid

^{1}H-NMR ($CDCl_3$): 1.15 (t, 3H); 1.7 (m, 2H); 1.95 (m, 4H); 2.15 (m, 2H); 2.65 (s, 3H); 3.65 (quin, 1H); 4.15 (t, 2H); 7.05 (d, 1H); 7.1 (t, 1H); 7.5 (td, 1H); 8.2 (dd, 1H).

EXAMPLE 18A

2-(2-Ethoxyphenyl)-5-methyl-7-(2-ethylpropyl)-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



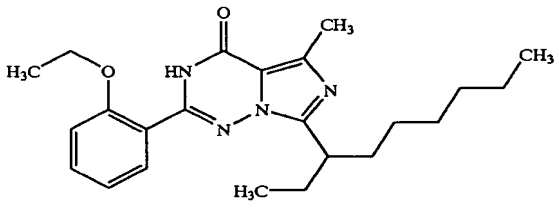
The preparation is carried out analogously to the procedure of Example 15A using 21.45 g (0.1 mol) of 2-(2-ethyl)-butyrylamino-propionic acid (Example 3A) and 20.6 g (0.1 mol) of 2-ethoxybenzamidine hydrochloride (Example 12A). The product is purified by silica gel chromatography using the mobile phase dichloromethane/methanol 60:1.

Yield: 7.22 g (21.3%)

200 MHz ^{1}H-NMR ($CDCl_3$): 0.87 (t, 6H); 1.57 (t, 3H); 1.88 (m, 4H); 2.67 (s, 3H); 3.28 (m, 1 h); 4.28 (q, 2H); 7.05 (d, 1H); 7.13 (dt, 1H); 8.15 (dd, 1H).

EXAMPLE 19A

2-(2-Ethoxyphenyl)-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one



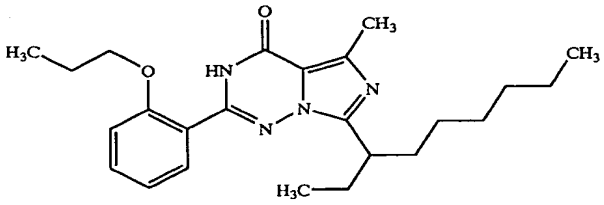
The preparation is carried out analogously to the procedure of Example 15A using 10.95 g (45 mmol) of 2-(2-ethyl)octanoylamino-propionic acid (Example 4A) and 9.03 g (45 mmol) of 2-ethoxybenzamidine hydrochloride (Example 12A). The product is purified by silica gel chromatography using the mobile phase dichloromethane/methanol 100:1.

Yield: 2.76 g (15.5%), yellow oil

^{1}H-NMR ($CDCl_3$): 0.75–0.9 (m, 6H); 1.1–1.4 (m, 8H); 1.5 (t, 3 h); 1.8–2.05 (m, 4 h); 2.7 (s, 3H); 3.4 (quin, 1H); 4.3 (t, 2H); 7.05–7.2 (pseudo quar 2 h); 7.5 (td, 1H); 8.2 (dd, 1H); 10.4 (broad, 1H).

EXAMPLE 20A

2-(2-Propoxyphenyl)-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one



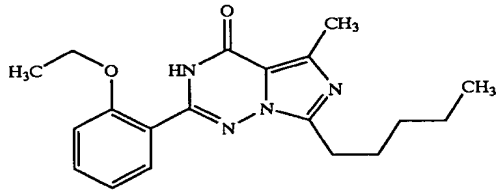
The preparation is carried out analogously to the procedure of Example 15A using 10.95 g (45 mmol of 2-(2-ethyl)-octanoylamino-propionic acid (Example 4A) and 9.66 g (45 mmol) of 2-propoxybenzamidine hydrochloride (Example 14A). The product is purified by silica gel chromatography using the mobile phase dichloromethane/methanol 60:1.

Yield: 3.7 g (20%), yellow oil

^{1}H-NMR ($CDCl_3$): 0.75–0.9 (m, 6H); 1.15 (t, 3 h); 1.1–1.35 (m, 8H); 1.75–2.1 (m, 6 h); 2.7 (s, 3H); 3.4 (quin, 1H); 4.2 (t, 2H); 7.05–7.2 (pseudo quar, 2H); 7.5 (td, 1H), 8.2 (dd, 1H); 10.2 (broad, 1H).

EXAMPLE 21A

2-(2-Ethoxyphenyl)-5-methyl-7-pentyl-3H-imidazo [5,1-f][1,2,4]triazin-4-one



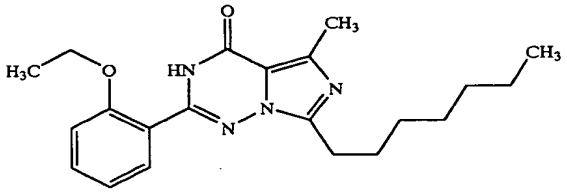
The preparation is carried out analogously to the procedure of Example 15A using 9.36 g (50 mmol of 2-hexanoylamino-propionic acid (Example 5A) and 10.1 g (50 mmol) of 2-ethoxybenzamidine hydrochloride (Example 12A). The product is purified by silica gel chromatography using the mobile phase dichloromethane/methanol 50:1.

Yield: 3.1 g (18.3%), oil

^{1}H-NMR (CD_3OD): 0.9 (t, 3H); 1.3–1.4 (m, 4 h); 1.45 (t, 3H); 1.8 (quin, 2H); 2.1 (s, 3H); 3.0 (t, 2H); 4.2 (quar, 2H); 7.1 (t, 1H); 7.15 (d, 1H); 7.5 (td, 1H); 7.7 (dd, 1H).

EXAMPLE 22A

2-(2-Ethoxyphenyl)-5-methyl-7-heptyl-3H-imdazo-[5,1-f][1,2,4]triazin-4-one

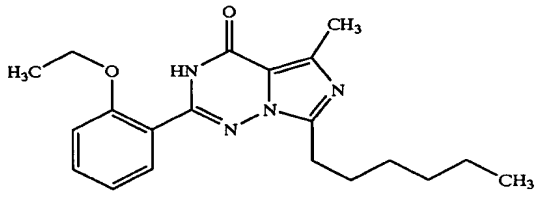


The preparation is carried out analogously to the procedure of Example 15A using 14.7 g (68.1 mmol) of 2-octanoylamino-propionic acid (Example 6A) and 13.66 g (68.1 mmol) of 2-ethoxybenzamidine hdyrochloride (Example 12A). The product is purified by silica gel chromatography using the mobile phase dichloromethane/methanol 50:1.

Yield: 4.65 g (18.5%), oil

^{1}H-NMR (CD_3OD): 0.85 (t, 3H); 1.2–1.4 (m, 8H); 1.45 (t, 3H); 2.8 (quin, 2H); 2.6 (s, 3H); 3.0 (t, 2H); 4.2 (quar, 2H); 7.1 (t, 1H); 7.2 (d, 1H); 7.55 (td, 1H), 7.7 (dd, 1H).

EXAMPLE 23A



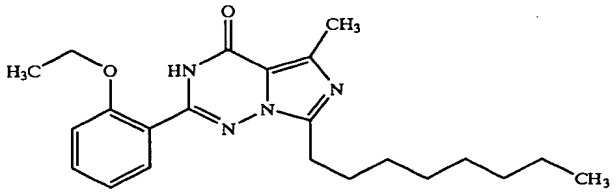
The preparation is carried out analogously to the procedure of Example 15A using 14.1 g (70 mmol) of 2-heptanoylamino-propionic acid (Example 7A) and 14.05 g (70 mmol) of 2-ethoxybenzamidine hydrochloride (Example 12A). The product is purified by silica gel chromatography using the mobile phase petroleum ether/ethyl acetate 1:1.

Yield: 3.5 g (14.1%)

^{1}H-NMR (CD_3OD): 0.9 (t, 3H); 1.3–1.45 (m, 6H); 1.4 (t, 3H); 1.7–1.9 (m, 2H); 2.15 (s, 3H); 3.1 (t, 2H); 4.2 (quar., 2H); 7.1 (t, 1H); 7.15 (d, 1H); 7.05 (td, 1H); 7.7 (dd, 1H).

EXAMPLE 24A

2-(2-Ethoxyphenyl)-5-methyl-7-n-3H-imidazo[5,1-f]-[1,2,4-]-triazin-4-one



The preparation is carried out analogously to the procedure of Example 15A using 17.0 g (70 mmol) of

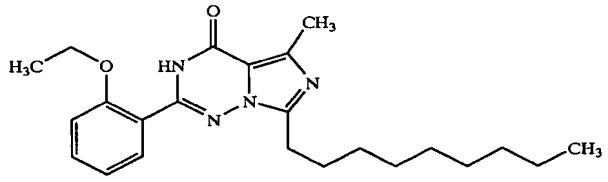
2-decanoylamino-propionic acid (Example 8A) and 14.05 g (70 mmol) of 2-ethoxybenzamidine hydrochloride (Example 12A). The product is purified by silica gel chromatography using the mobile phase petroleum ether/ethyl acetate 1:1.

Yield: 3.5 g (14.1%)

^{1}H-NMR (CD_3OD): 0.9 (t, 3H); 1.3–1.45 (m, 6H); 1.4 (t, 3H); 1.7–1.9 (m, 2H); 2.15 (s, 3H); 3.1 (t, 2H); 4.2 (quar., 2H); 7.1 (t, 1H); 7.15 (d, 1H); 7.05 (td, 1H), 7.7 (dd, 1H).

EXAMPLE 24B

2-(2-Ethoxyphenyl)-5-methyl-7-n-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



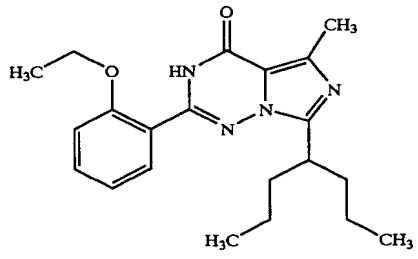
The preparation is carried out analogously to the procedure of Example 15A using 17.0 g (70 mmol) of 2-decanoylamino-propionic acid (Example 8A) and 14.05 g (70 mmol) of 2-ethoxybenzamidine hydrochloride (Example 12A). The product is purified by silica gel chromatography using the mobile phase methylene chloride/methanol 50:1. The product can then be crystallized from petroleum ether.

Yield: 4.64 g (16.7%)

H-NMR (CD_3OD): 0.85 (t, 3H); 1.2–1.4 (m, 12H), 1.45 (t, 3H); 1.86 (quin., 2H); 2.6 (s, 3H); 3.0 (t, 2H); 4.2 (quar., 2H); 7.05 (t, 1H); 7.15 (d, 1H); 7.5 (td, 1H); 7.7 (dd, 1H).

EXAMPLE 25A

2-(2-Ethoxyphenyl)-5-methyl-7-(2-n-propylbutyl)-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



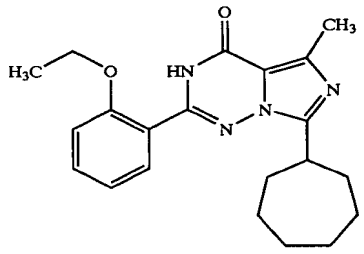
The preparation is carried out analogously to the procedure of Example 15A using 10.72 g (49.8 mmol) of 2-(2-n-propyl)-pentanoylamino-propionic acid (Example 9A) and 10.0 g (49.8 mmol) of 2-ethoxybenzamidine hydrochloride (Example 12A). The product is purified by silica gel chromatography using the mobile phase methylene chloride/methanol 100:1, then 50:1. The product can be recrystallized from diethyl ether.

Yield: 1.8 g (9.8%)

M.p.: 150° C.

EXAMPLE 26A

2-(Ethoxyphenyl)-5-methyl-7-cycloheptyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



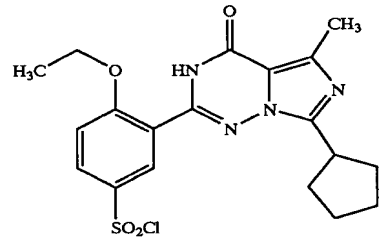
The preparation is carried out analogously to the procedure of Example 15A using 14.9 g (70 mmol) of 2-cycloheptanoylamino-propionic acid (Example 10A) and 14 g (70 mmol) of 2-ethoxybenzamidine hydrochloride (Example 12A). The product is purified by silica gel chromatography using the mobile phase methylene chloride/methanol 10:1, and then 50:1.

Yield: 5.35 g (20.9%)

^{1}H-NMR (CD_3OD): 1.45 (t, 3H); 1.6–2.0 (m, 10H); 2.1–2.2 (m, 2H); 2.7 (s, 3H); 3.65 (quin., 1H); 4.2 (quar., 2H); 7.1 (t, 1H); 7.2 (d, 1H); 7.6 (td, 1H); 7.75 (dd, 1H).

EXAMPLE 27A

4-Ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro-imidazo[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride



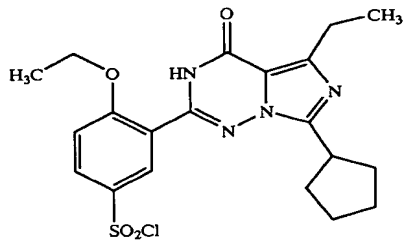
At 0° C., 7.0 g (20.7 mmol) of 2-(2-ethoxyphenyl)-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one (Example 15A) are added carefully to 24.1 g (207 mmol) of chlorosulphuric acid. The mixture is allowed to warm to room temperature and stirred overnight. The solution is carefully added to 200 ml of ice-water and extracted twice with dichloromethane. The combined organic phases are dried over sodium sulphate and the solvent is distilled off under reduced pressure. The sulphonyl chloride is dried under reduced pressure and reacted further to the sulphonamides without further purification.

Yield: 7.95 g (88%), white foam

^{1}H-NMR ($CDCl_3$): 1.6 (t, 3H); 1.7 (m, 2H); 1.95 (m, 4H); 2.15 (m, 2H); 2.65 (s, 3H); 3.71 (quin, 1H); 4.4 (quar, 2H); 7.25 (d, 1H); 8.2 (dd, 1H); 8.7 (d, 1H); 9.9 (s, 1H).

EXAMPLE 28A

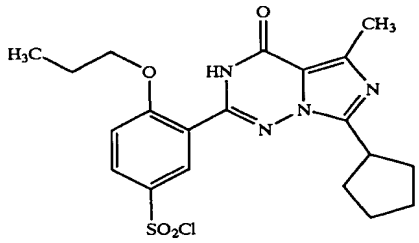
4-Ethoxy-3-(5-ethyl-4-oxo-7-cyclopentyl-3,4-dihydro-imidazo[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride



The preparation is carried out analogously to the procedure of Example 27A using 0.34 g (0.96 mmol) of 2-(2-ethoxyphenyl)-5-ethyl-7-cyclopentyl-3H-imidazo[5.1-f][1,2,4]triazin-4-one (Example 16A). This gives 0.43 g (98%) of sulphonyl chloride as a colourless foam which is directly reacted further.

EXAMPLE 29A

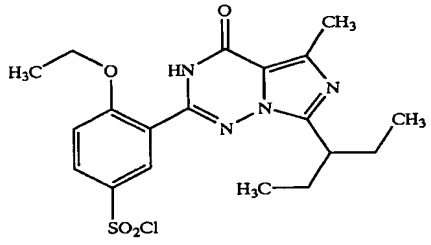
4-Propoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro-imidazo[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride



The preparation is carried out analogously to the procedure of Example 27A using 0.7 g (2 mmol) of 2-(2-propoxyphenyl)-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][12,4]triazin-4-one (Example 17A). This gives 0.8 g (89.3%) of sulphonyl chloride as a white foam which is directly reacted further.

EXAMPLE 30A

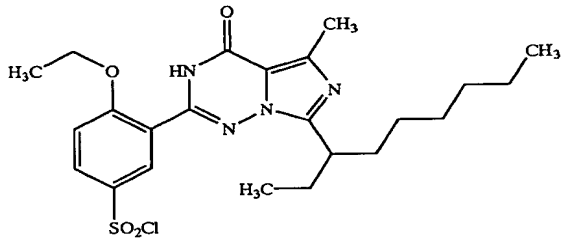
4-Ethoxy-3-(5-methyl-4-oxo-7-(2-ethylpropyl)-3,4-dihydro-imidazo[5,1-f][1,2,4]-triazin-2-yl-benzenesulphonyl chloride



The preparation is carried out analogously to the procedure of Example 27A using 7.23 g (0.12 mmol) of 2-(2-ethoxyphenyl)-5-methyl-7-(2-ethylpropyl)-3H-imidazo[5,1-f][1,2,4]-triazin-4-one (Example 18A). This gives 8.56 g (91.9%) of sulphonyl chloride as a white solid which is directly reacted further.

EXAMPLE 31A

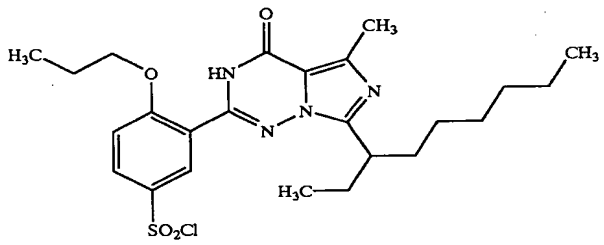
4-Ethoxy-3-(5-methyl-4-oxo-7-(2-ethylheptyl)-3,4-dihydro-imidazo[5,1f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride



The preparation is carried out analogously to the procedure of Example 27A using 5.6 g (14.1 mmol) of 2-(2-ethoxyphenyl)-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f][1,2,4]-triazin-4-one (Example 19A). This gives 3.7 g (52.9%) of sulphonyl chloride as a slightly yellow foam which is directly reacted further.

EXAMPLE 32A

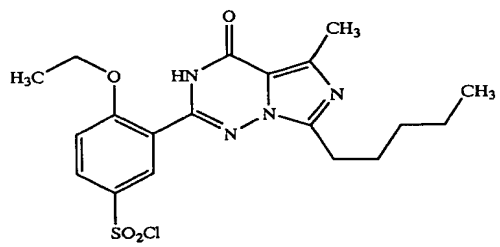
4-Propoxy-3-(5-methyl-4-oxo-7-(2-ethylheptyl)-3,4-dihydro-imidazo[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride



The preparation is carried out analogously to the procedure of Example 27A using 1.4 g (3.41 mmol) of 2-(2-propoxyphenyl)-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f]-[1,2,4]-triazin-4-one (Example 20A). This gives 1.4 g (80.6%) of sulphonyl chloride as a white foam which is directly reacted further.

EXAMPLE 33A

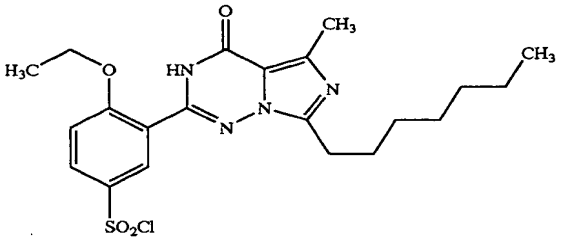
4-Ethoxy-3-(5-methyl-4-oxo-7-pentyl-3H-imidazo-[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride



The preparation is carried out analogously to the procedure of Example 27A using 0.3 g (0.88 mmol) of 2-(2-ethoxyphenyl)-5-methyl-7-pentyl-3H-imidazo[5,1-f][1,2,4]triazin4-one (Example 21A). This gives 0.3 g (77.6%) of sulphonyl chloride as a white foam which is directly reacted further.

EXAMPLE 34A

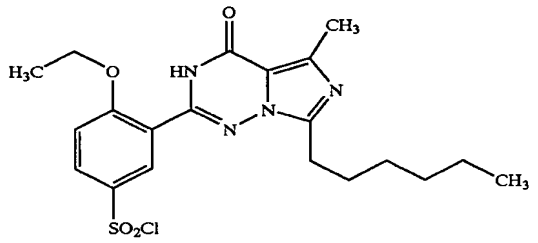
4-Ethoxy-3-(5-methyl-4-oxo-7-heptyl-3H-imidazo [5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride



The preparation is carried out analogously to the procedure of Example 27A using 0.3 g (0.81 mmol) of 2-(2-ethoxyphenyl)-5-methyl-7-heptyl-3H-imidazo[5,1-f][1,2,4] triazin-4-one (Example 22A). This gives 0.3 g (78.9%) of sulphonyl chloride as a white foam which is directly reacted further.

EXAMPLE 35A

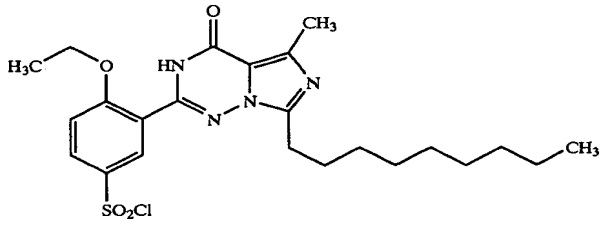
4-Ethoxy-3-(5-methyl-4-oxo-7-n-hexyl-3,4-dihydro-imidazo[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride



The preparation is carried out analogously to the procedure of Example 27A using 300 mg (0.84 mmol) of 2-(2-ethoxyphenyl)-5-methyl-7-n-hexyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one (Example 23A) and 0.98 g (8.4 mmol) of chlorosulphuric acid. This gives 300 mg (78.7%) of sulphonyl chloride which is directly reacted further.

EXAMPLE 36A

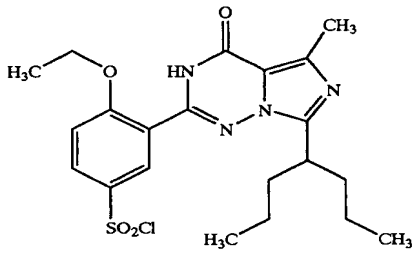
4-Ethoxy-3-(5-methyl-4-oxo-7-n-nonyl-3,4-dihydro-imidazo[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride



The preparation is carried out analogously to the procedure of Example 27A using 400 mg (1 mmol) of 2-(2-ethoxyphenyl)-5-methyl-7-n-nonyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one (Example 24A) and 1.18 g (10 mmol) of chlorosulphuric acid. This gives 402 mg (80.1%) of sulphonyl chloride which is directly reacted further.

EXAMPLE 37A

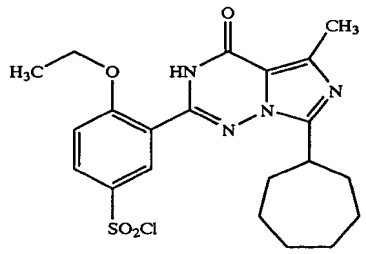
4-Ethoxy-3-(5-methyl-4-oxo-7-(2-n-propylbutyl)-3, 4-dihydro-imidazo[5,1-f][1,2,4]-triazin-2-yl-benzenesulphonyl chloride



The preparation is carried out analogously to the procedure of Example 27A using 300 mg (0.81 mmol) of 2-(2-ethoxyphenyl)-5-methyl-7-(2-n-propylbutyl)-3H-imidazo [5,1-f][1,2,4]-triazin-4-one (Example 25A) and 950 mg (8.1 mmol) of chlorosulphuric acid. This gives 300 g (78.9%) of sulphonyl chloride which is directly reacted further.

EXAMPLE 38A

4-Ethoxy-(5-methyl-4-oxo-7-cycloheptyl-3,4-dihydro-imidazo[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride

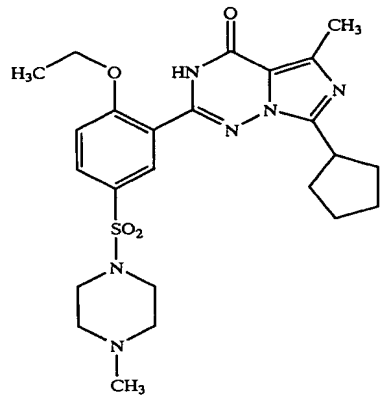


The preparation is carried out analogously to the procedure of Example 27A using 400 mg (1.1 mmol) of 2-(2-ethoxyphenyl)-5-methyl-7-cycloheptyl-3H-imidazo[5,1-f] [1,2,4]triazin-4-one (Example 26A) and 1.27 g (11 mmol) of chlorosulphuric acid. This gives 402 mg (78.6%) of sulphonyl chloride which is directly reacted further.

PREPARATION EXAMPLES

Example 1

2-[2-Ethoxy-5-(4-methylpiperazine-1-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



60 mg (0.137 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f]-[1,2,4]triazin-2-yl)-benzenesulphonyl chloride are dissolved in 10 ml of dichloromethane. 30 mg (0.343 mmol) of N-methylpiperazine are added, and the mixture is stirred at room temperature overnight. The mixture is washed twice with saturated ammonium chloride solution, dried over sodium sulphate and evaporated. The residue is purified by silica gel flash chromatography (dichloro methane/methanol 50:1).

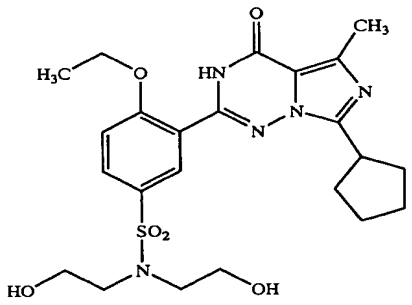
Yield: 52 mg (75.6%)

R_f=0.52 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 1.45 (t, 3H); 1.6–1.75 (m, 2H); 1.8–2.0 (m, 4H); 2.05–2.2 (m, 2H); 2.3 (s, 3H); 2.5–2.55 (m, 4H); 2.6 (m, 3H); 3.0 (s broad, 3H); 3.6 (quin, 1H); 4.3 (quar, 2H); 7.4 (d, 1H); 7.6 (dd, 1H); 8.0 (d, 1H).

Example 2

2-[2-Ethoxy-5-(N,N-bis-2-hydroxyethyl-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



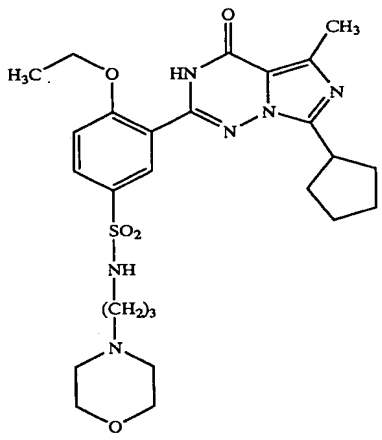
The preparation is carried out analogously to the procedure of Example 1 using 800 mg (1.83 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro-[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride and 420 mg (4.03 mmol) of N,N-bis-2-hydroxyethylamine. This gives 530 mg (57.3%) of sulphonamide.

R_f=0.51 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 1.45 (t, 3H); 1.65–1.75 (m, 2H); 1.8–1.95 (m, 4H); 2.05–2.2 (m, 2H); 2.6 (s, 3H); 3.2–3.3 (m, 4H); 3.6 (quin 1H); 3.7 (t, 4H); 4.3 (quar, 2H); 7.35 (d, H); 8.0 (dd, 1H); 8.13 (d, 1H).

Example 3

2-[2-Ethoxy-5-(3-(4-morpholino)-propyl)-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



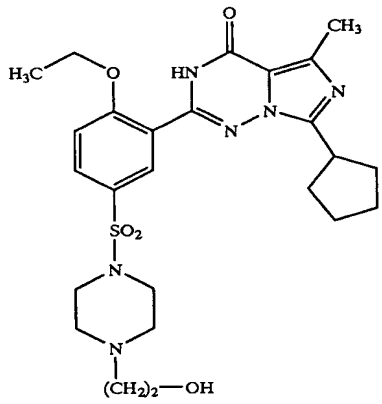
The preparation is carried out analogously to the procedure of Example 1 using 2.0 g (4.58 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 2.2 g (10.07 mmol) of 4-(3-aminopropyl)-morpholine. This gives 1.67 g (67%) of sulphonamide.

R_f=0.45 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 1.45 (t, 3H); 1.55–2.2 (m, 10H); 2.3–2.45 (m, 4H); 2.6 (s, 3H); 2.9 (t, 2H); 3.55–3.7 (m, 4H); 4.3 (quar. 2H); 7.3 (d, 1H); 8.0 (dd,); 8.1 (d, 1H).

Example 4

2-[2-Ethoxy-5-(4-(2-hydroxyethyl)-piperazine-1-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



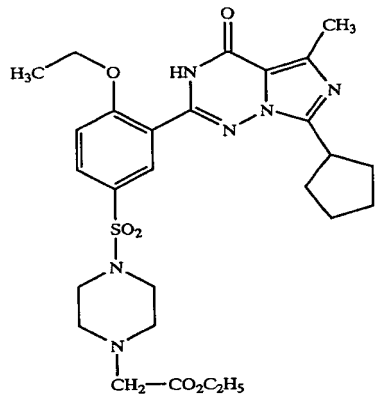
The preparation is carried out analogously to the procedure of Example 1 using 2.0 g (4.58 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 2.2 g (10.1 mmol) of N-(2-hydroxyethyl)piperazine. This gives 1.8 g (74.1%) of sulphonamide.

R_f=0.51 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 1.45 (t, 3H); 1.6–2.2 (m, 8H); 2.5 (t, 2H); 2.55–2.65 (m, 7H); 3.0–3.1 (m, 4H); 3.6 (t, +quin. 3H); 4.3 (quar. 2H); 7.35 (d, 1H); 7.9 (dd, 1H); 8.0 (d, 1H).

Example 5

2-[2-Ethoxy-5-(4-N-ethoxycarbonylmethyl-piperazine-1-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



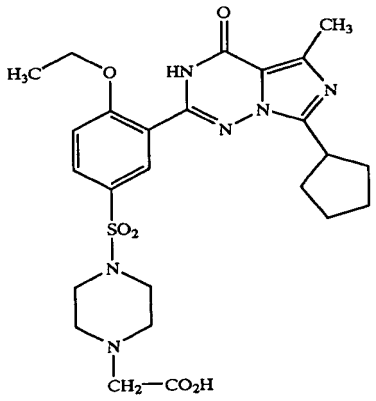
The preparation is carried out analogously to the procedure of Example 1 using 100 mg (0.23 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 90 mg (0.504 mmol) of N-(carboethoxymethyl)piperazine. This gives 57 mg (43.5%) of sulphonamide.

R_f=0.53 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 1.25 (t, 3H); 1.45 (t, 3H); 1.65–2.2 (m, 8H); 2.5 (s, 3H); 2.6–2.7 (m, 4H); 3.0–3.1 (m, 4H); 3.25 (s, 2H); 3.6 (quin., 1H); 4.15 (quar, 2 h); 4.3 (quar, 2H); 7.35 (d, 1H); 7.95 (dd, 1H); 8.0 (d, 1H).

Example 6

2-[2-Ethoxy-5-(4-N-carboxymethyl-piperazine-1-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



50 mg (0.084 mmol) of the ester from Example 5 and 10 mg (0.335 mmol) of sodium hydride are stirred at room temperature in 4 ml of methanol/water 3:1 for 30 minutes. The mixture is evaporated and the residue is purified by silica gel chromatography (mobile phase: methanol/dichloromethane 10:1).

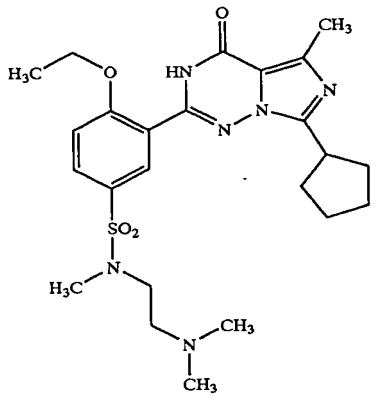
Yield: 39 mg (85.4%)

R_f=0.671 (CH_2Cl_2/MeOH 10:1+1% AcOH)

^{1}H-NMR (CD_3OD): 1.45 (t, 3H); 1.65–2.2 (m, 2H); 2.1 (s, 3H); 2.15–2.25 (m, 4H); 3.05 (s, 2H); 3.05–3.15 (m, 4H); 3.6 (quin, 1H); 4.3 (quar, 2H); 7.4 (d, 1H); 7.95 (dd, 1H); 8.05 (d, 1H).

Example 7

2-[2-Ethoxy-5-(N-methyl-N-(2-dimethylaminoethyl)-sulphonamido)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



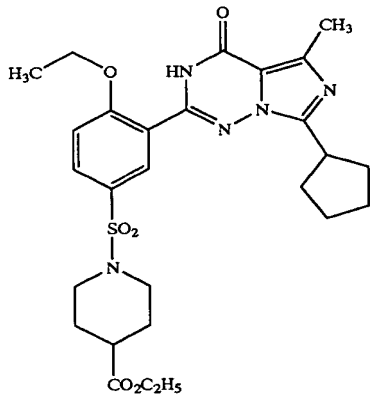
The preparation is carried out analogously to the procedure of Example 1 using 60 mg (0.137 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 40 mg (0.343 mmol) of N-methyl-N-(2-dimethylamino-ethyl)-amine. This gives 52 mg (75.3%) of sulphonamide.

R_f=0.29 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 1.45 (t, 3H); 1.65–2.2 (m, 8H); 2.3 (s, 6H); 2.55 (t, 2H); 2.6 (s, 3H); 2.8 (s, 3H); 3.15 (t, 2H); 3.6 (quin, 1H); 4.3 (quar, 2H); 7.4 (d, 1H); 7.95 (dd, 1H); 8.1 (d, 1H).

Example 8

2-[2-Ethoxy-5-(4-ethoxycarbonylpiperidine-1-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one

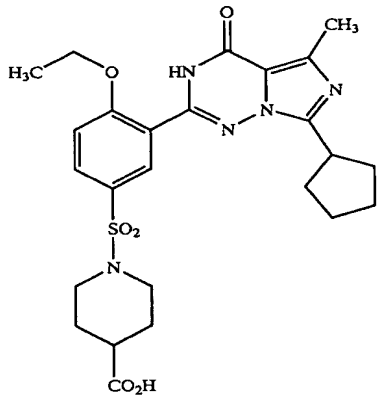


The preparation is carried out analogously to the procedure of Example 1 using 200 mg (0.458 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 160 mg (1 mmol) of methyl piperidine-4-carboxylate. This gives 190 mg (74.4%) of sulphonamide.

^{1}H-NMR (CD_3OD): 1.2 (t, 3H); 1.45 (t, 3H); 1.65–2.2 (m, 10H); 2.3 (m, 1H); 2.5–2.6 (m, 2H); 2.6 (s, 3H); 3.55–3.7 (m, 3H); 4.1 (quar, 2H); 4.3 (quar, 2H); 7.4 (d, 1H); 7.9 (dd, 1H); 8.0 (d, 1H).

Example 9

2-[2-Ethoxy-5-(4-carboxypiperidine-1-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f] [1,2,4]-triazin-4-one



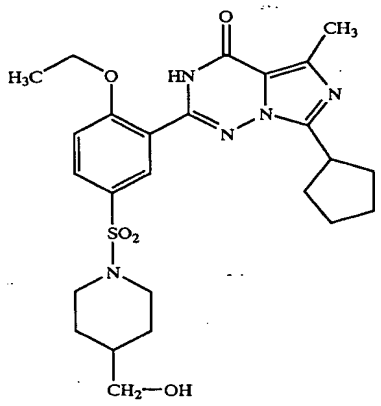
180 mg (0.323 mmol) of the ester from Example 8 and 50 mg (1.29 mmol) of sodium hydroxide are stirred at room temperature in 20 ml of methanol/water 3:1 for 30 minutes. 10 ml of water are added and the mixture is extracted once with dichloromethane. The aqueous phase is acidified using 2 n HCl and extracted twice with dichloromethane. The combined dichloromethane phases are dried over sodium sulphate and evaporated. The residue is recrystallized from diethyl ether.

Yield: 120 mg (70.2%)

M.p.: 170° C. (decomp.)

Example 10

2-[2-Ethoxy-5-(4-hydroxymethylpiperidine-1-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one

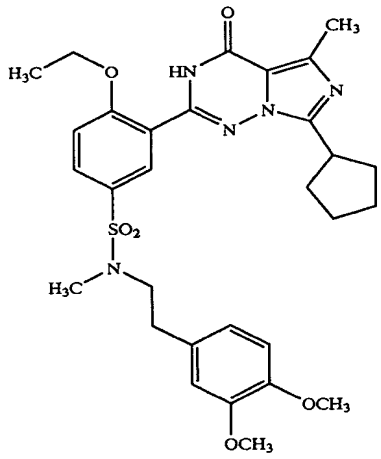


The preparation is carried out analogously to the procedure of Example 1 using 60 mg (0.137 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 30 mg (0.302 mmol) of 4-hydroxymethylpiperidine. This gives 55 mg (77.7%) of sulphonamide.

R_f=0.46 (toluene/acetone 1:1)

Example 11

2-[2-Ethoxy-5-(N-methyl-N-(2-(3,4-dimethoxyphenyl)ethyl)-sulphonamido)phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



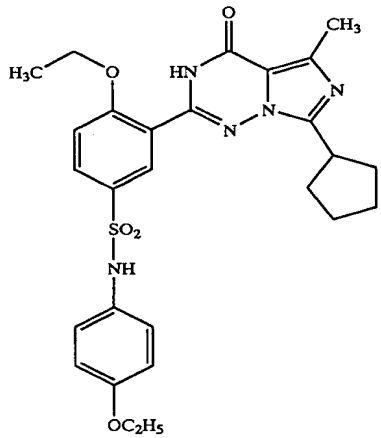
The preparation is carried out analogously to the procedure of Example 1 using 60 mg (0.137 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 60 mg (0.302 mml) of N-methyl-N-(2-(3,4-dimethoxyphenyl)ethylamine. This gives 66 mg (80.9%) of sulphonamide.

R_f=0.64 (toluene/acetone 1:1)

^{1}H-NMR (CD_3OD): 1.45 (t, 3H); 1.6–2.15 (m, 8H); 2.55 (s, 3H); 2.75 (s, 3H); 2.8 (t, 2H); 3.3 (t, 2H); 3.55 (quin, 1H); 3.8 (s, 6H); 4.25 (quar, 2H); 6.7–6.85 (m, 3H); 7.3 (d, 1H); 7.9 (dd, 1H); 8.0 (d, 1H).

Example 12

2-[2-Ethoxy-5-(4-ethoxyphenyl-sulphonamido)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f] [1,2,4]-triazin-4-one



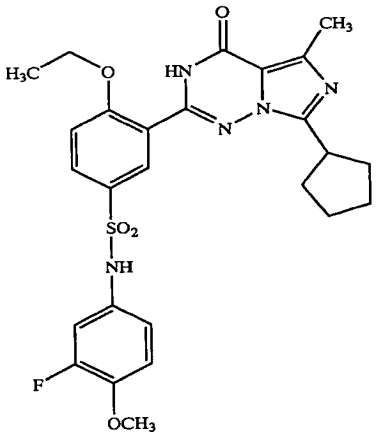
The preparation is carried out analogously to the procedure of Example 1 using 100 mg (0.229 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 70 mg (0.504 mmol) of 4-ethoxy-aniline. This gives 62 mg (50.4%) of sulphonamide which is purified by recrystallization from ethyl acetate/petroleum ether.

Yield: 62 mg (50.4%)

M.p.: 245° C.

Example 13

2-[2-Ethoxy-5-(3-fluoro-4-methoxyphenyl-sulphonamido)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



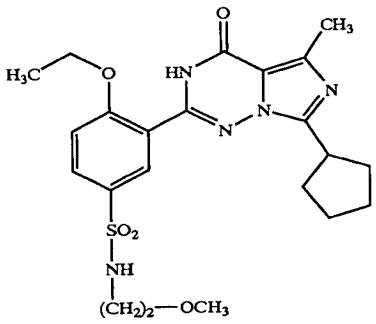
The preparation is carried out analogously to the procedure of Example 1 using 100 mg (0.229 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 70 mg (0.5 mmol) of 3-fluoro-4-methoxyaniline. This gives 73 mg (58.9%) of sulphonamide which is purified by recrystallization from diethyl ether.

Yield: 73 mg (58.9%)

M.p.: 180° C. (decomp.)

Example 14

2-[2-Ethoxy-5-(2-methoxyethyl-sulphonamido)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



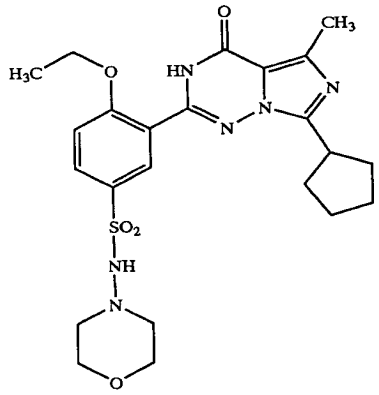
The preparation is carried out analogously to the procedure of Example 1 using 100 mg (0.229 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 37.5 mg (0.05 mmol) of 2-methoxy-ethylamine. This gives 80 mg (73.2%) of sulphonamide.

R_f=0.47 (toluene/acetone 4:1)

^{1}H-NMR (C_3OD): 1.45 (t, 3H); 1.65–2.2 (m, 8H); 2.6 (s, 3H); 3.05 (t, 2H); 3.25 (s, 3H); 3.4 (t, 2H); 3.65 (quin, 1H); 4.3 (quin, 2H); 7.3 (d, 1H); 8.0 (dd, 1H); 8.1 (d, 1H).

Example 15

2-[2-Ethoxy-5-(N-(4-morpholinyl)-sulphonamido)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



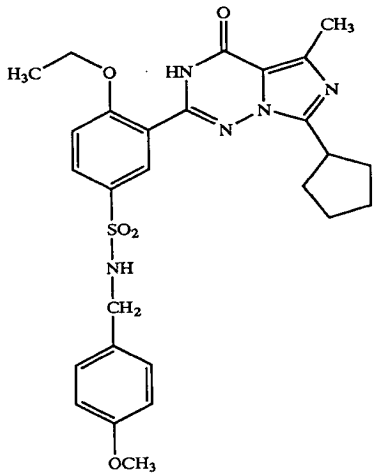
The preparation is carried out analogously to the procedure of Example 1 using 100 mg (0.229 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 50 mg (0.5 mmol) of 4-aminomorpholine. This gives 108 mg (93.9%) of sulphonamide.

R_f=0.24 (toluene/acetone 4:1)

^{1}H-NMR (CD_3OD): 1.45 (t, 3H); 1.65–2.2 (m, 8H); 2.6 (s, 3H); 2.9–3,0 (m, 4H); 3.65 (quin, 1H); 3.65–3.75 (m, 4H); 4.3 (quar, 2H); 7.4 (d, 1H); 7.95 (dd, 1H); 8.05 (d, 1H).

Example 16

2-[2-Ethoxy-5-(4-methoxybenzyl-sulphonamido)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



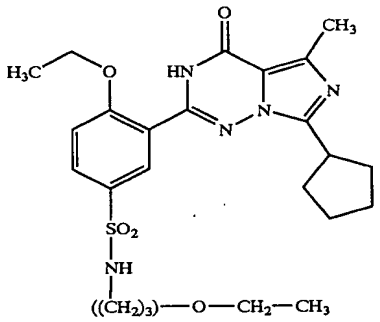
The preparation is carried out analogously to the procedure of Example 1 using 400 mg (0.915 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 310 mg (2.29 mmol) of 4-methoxybenzylamine. This gives 260 mg (52.8%) of sulphonamide.

R_f=0.25 (toluene/acetone 4:1)

^{1}H-NMR (CD_3OD): 1.45 (t, 3H); 1.65–1.75 (m, 2H); 1.8–1.95 (m, 4H); 2.1–2.2 (m, 2H); 2.55 (s, 3H); 3.63 (quin, 1H); 3.67 (s, 3H); 4.05 (s, 2H); 4.25 (quar, 2H); 6.75 (d, 2H); 7.1 (d, 2H); 7.25 (d, 1H); 7.9 (dd, 1H); 7.95 (d, 1H).

Example 17

2-[2-Ethoxy-5-(3-ethoxypropyl-sulphonamido)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



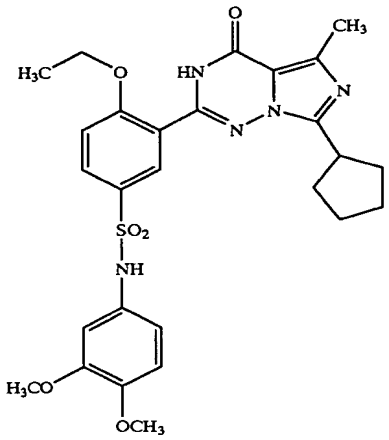
The preparation is carried out analogously to the procedure of Example 1 using 300 mg (0.687 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 180 mg (1.717 mmol) of 3-ethoxy-propylamine. This gives 230 mg (66.5%) of sulphonamide.

R_f=0.19 (toluene/acetone)

^{1}H-NMR (CD_3OD): 1.1 (t, 3H); 1.45 (t, 3H); 1.65–2.2 (m 10H); 2.6 (s, 3H; 2.95 (t, 2H); 3.35–3.5 (m, 4H); 3.65 (quin, 1H); 4.25 (quar, 2H); 7.3 (d, 1H); 7.95 (dd, 1H); 8.1 (d, 1H).

Example 18

2-[2-Ethoxy-5-(3,4-dimethoxyphenyl-sulphonamido)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



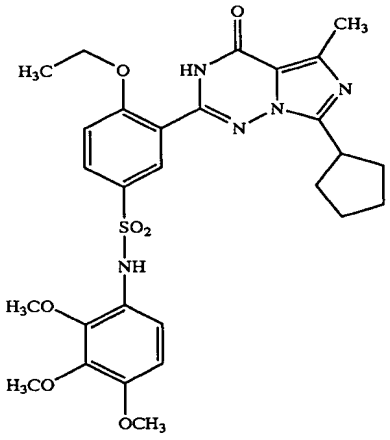
The preparation is carried out analogously to the procedure of Example 1 using 100 mg (0.229 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 80 mg (0.5 mmol) of 3,4-dimethoxyaniline. This gives 70 mg (55.2%) of sulphonamide.

R_f=0.17 (toluene/acetone 4:1)

^{1}H-NMR (CD_3OD): 1.45 (t, 3H); 1.75–1.95 (m, 6H); 2.15–2.3 (m, 2H), 2.7 (s, 3H); 3.65–3.8 (m, 7H); 4.2 (quar, 2H); 6.55 (dd, 1H); 6.7–6.8 (m, 2H); 7.3 (d, 1H); 7.9–8.0 (m, 2H).

Example 19

2-[2-Ethoxy-5-(2,3,4-trimethoxyphenyl-sulphonamido)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



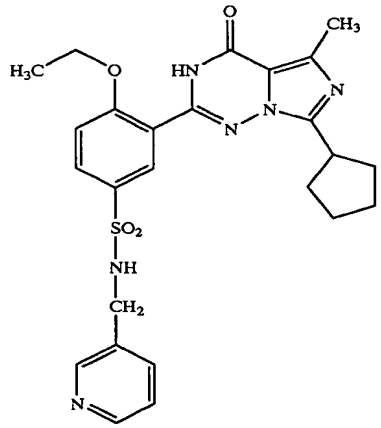
The preparation is carried out analogously to the procedure of Example 1 using 100 mg (0.229 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 90 mg (0.5 mmol) of 2,3,4-trimethoxyaniline. This gives 61 mg (45.7%) of sulphonamide.

R_f=0.25 (toluene/acetone 4:1)

^{1}H-NMR (CD_3OD): 1.4 (t, 3H); 1.65–1.95 (m, 6H); 2.05–2.2 (m, 2H); 2.55 (s, 3H); 3.5 (s, 3H); 36 (quin, 1H); 3.7 (s, 3H); 3.8 (s, 3H); 4.2 (quar, 2H); 6.7 (d, 1H); 7.15 (d, 1H); 7.2 (d, 1H); 7.8 (dd, 1H); 8.0 (d, 1H).

Example 20

2-[2-Ethoxy-5-(3-picolyl-sulphonamido)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one

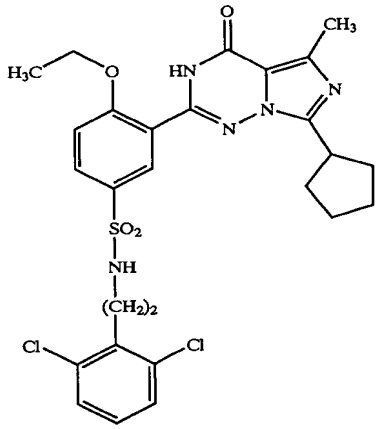


The preparation is carried out analogously to the procedure of Example 1 using 100 mg (0.229 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 50 mg (0.5 mmol) of 3-picolylamine. This gives 50 mg (43%) of sulphonamide which is purified by recrystallization from ethyl acetate/diethyl ether.

M.p.: 128–130° C. (decomp.)

Example 21

2-[2-Ethoxy-5-(2-(2,6-dichlorophenyl)ethyl-sulphonamido)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one

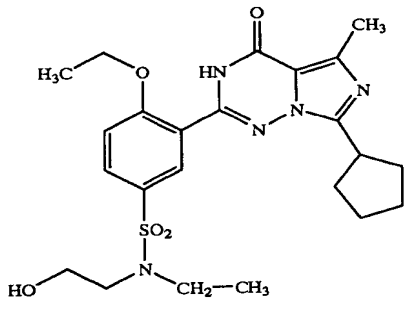


The preparation is carried out analogously to the procedure of Example 1 using 400 mg (0.915 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1- f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 440 mg (2.29 mmol) of 2-(2,6-dichlorophenyl)ethylamine. This gives 380 mg (70.3%) of sulphonamide which is purified by recrystallization from ethyl acetate/diethyl ether.

M.p.: 202° C.

Example 22

2-[2-Ethoxy-5-(N-ethyl-N-(2-hydroxyethyl)-sulphonamido)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one

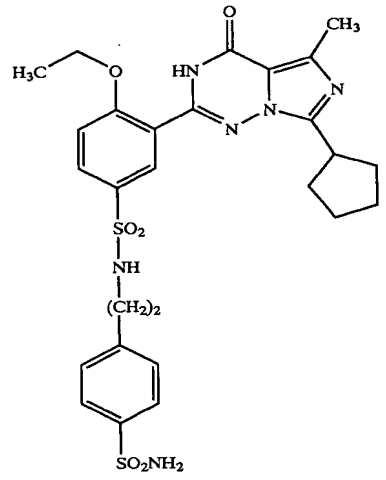


The preparation is carried out analogously to the procedure of Example 1 using 100 mg (0.229 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 50 mg (0.57 mmol) of N-ethyl-N-(2-hydroxyethyl)amine. This gives 57 mg (50.9%) of sulphonamide which is recrystallization from ethyl acetate/diethyl ether.

M.p.: 193° C.

EXAMPLE 23

2-[2-Ethoxy-5-(2-(4-sulphonamidophenyl)-ethyl-sulphonamido)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one

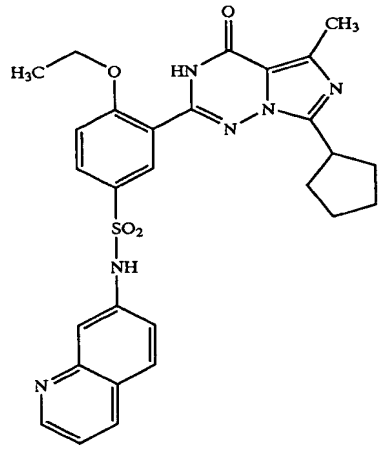


The preparation is carried out analogously to the procedure of Example 1 using 100 mg (0.229 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 110 mg (0.572 mmol) of 2-(4-sulphonamidophenyl)-ethylamine. This gives 67 mg (48.7%) of sulphonamide which is purified by recrystallization from ethyl acetate/diethyl ether.

M.p.: 141–143° C. (decomp.)

EXAMPLE 24

2-[2-Ethoxy-5-(7-quinolinyl-sulphonamido)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



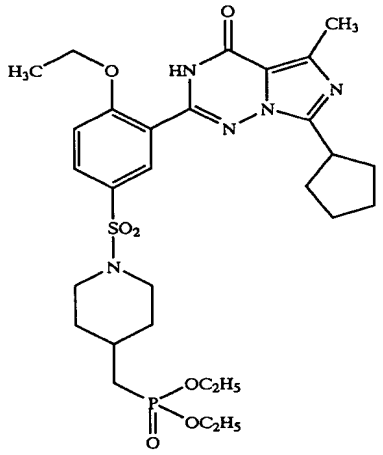
The preparation is carried out analogously to the procedure of Example 1 using 400 mg (0.915 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 290.4 mg (2.014 mmol) of 7-aminoquinoline. This gives 264 mg

(52.9%) of sulphonamide which is purified by recrystallization from ethyl acetate.

M.p.: 184° C.

EXAMPLE 25

2-[2-Ethoxy-5-(1-(4-diethoxyphosphonylmethyl-piperidinyl)-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one

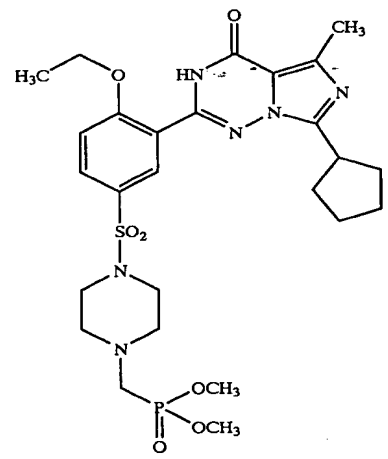


The preparation is carried out analogously to the procedure of Example 1 using 100 mg (0.229 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride and 120 mg (0.5 mmol) of 4-dimethoxyphosphonyl-methyl-piperidine. This gives 62 mg (42.6%) of sulphonamide.

^{1}H-NMR (CD_3OD): 1.25 (t, 6H); 1.45 (t, 3H); 1.5–2.2 (m, 15H); 2.3 (t, 2H); 2.6 (s, 3H); 3.5–3.8 (m, 3H); 4.05 (m, 4H); 4.8 (quar, 2H); 7.35 (d, 1H); 7.9 (dd, 1H); 8.0 (d, 1H).

EXAMPLE 26

2-[2-Ethoxy-5-(1-(4-dimethoxyphosphonylmethyl-piperazinyl-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



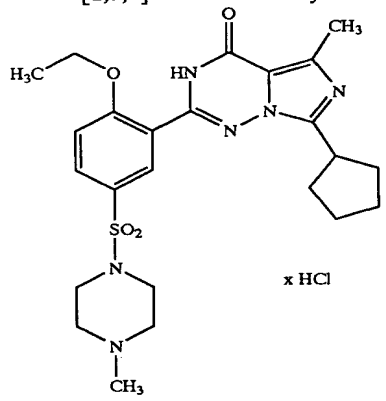
The preparation is carried out analogously to the procedure of Example 1 using 100 mg (0.229 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride and 100 mg (0.5 mmol) of (4-dimethoxyphosphonylmethyl)-piperazine. This gives 53 mg (38%) of sulphonamide.

R_f=0.57 (dichloromethane/methanol 10:1)

^{1}H-NMR (CD_3OD): 1.45 (t, 3H); 1.65–2.0 (m, 6H); 2.05–2.2 (m, 2H); 2.55 (s, 3H); 2.65–2.75 (m, 4H); 2.9 (d, 3H); 3.0–3.1 (m, 4H); 3.6 (quin, 1H); 3.7 (s, 3H); 3.75 (s, 6H); 4.3 (quar, 2H); 7.35 (d, 1H); 7.9 (dd, 1H); 8.0 (d, 1H).

EXAMPLE 27

2-[2-Ethoxy-5-(methylpiperazine-1-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one hydrochloride

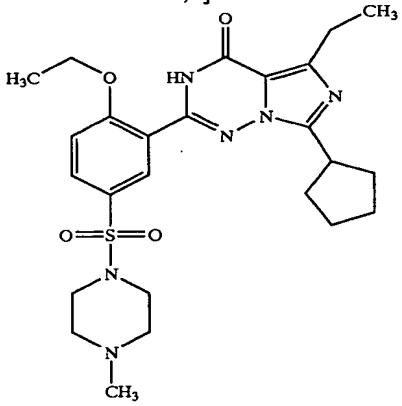


220 mg (0.42 mmol) of 2-[2-ethoxy-5-(4-methylpiperazine-1-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,-f][1,2,4]-triazin-4-one (Example 1) are suspended in 20 ml of diethyl ether and, after addition of 20 mg (0.462 mmol) of 1 molar ethereal HCl solution, stirred at room temperature for 30 minutes. The solvent is distilled off under reduced pressure and the residue is dried under high vacuum.

Yield: 236 mg (99%)

EXAMPLE 28

2-[2-Ethoxy-5-(4-methylpiperazine-1-sulphonyl)-phenyl]-5-ethyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one



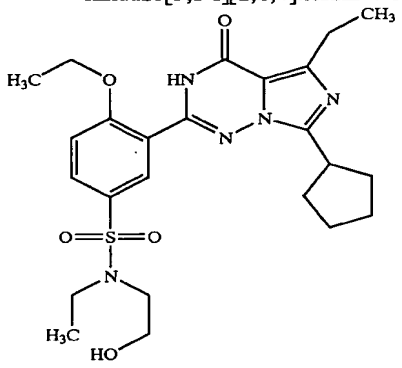
0.42 g (0.92 mmol) of 3-(7-cyclopentyl-5-ethyl-4-oxo-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)-4-

ethoxybenzenesulphonyl chloride are dissolved in 15 ml of dichloromethane and cooled to 0° C. After addition of a spatula tip of 4-dimethylaminopyridine, 0.28 g (2.76 mmol) of N-methylpiperazine are added, and the reaction mixture is stirred at room temperature overnight. The mixture is diluted with dichloromethane, the organic phase is washed with ammonium chloride solution and dried over sodium sulphate and the solvent is removed under reduced pressure. Crystallization from ether gives 0.395 g (80%) of a colourless solid.

200 MHz ^{1}H-NMR (DMSO-d_6): 1.21 (t, 3H); 1.32 (t, 3H); 1.79 (m, 8H); 2.13 (s, 3H); 2.48 (s, 4H); 2.86 (m, 6H); 4.21 (quart., 2H); 7.48 (m, 1H); 7.85 (m, 2H); 11.70 (s, 1H).

EXAMPLE 29

2-[2-Ethoxy-5-N-ethyl-N-(2-hydroxyethyl)-amino-1-sulphonyl)-phenyl]-5-ethyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one



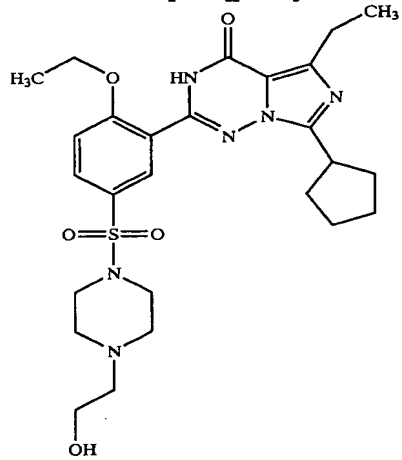
In an analogous manner, starting from 1.35 g (3 mmol) of 3-(7-cyclopentyl-5-ethyl-4-oxo-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxybenzene-sulphonyl chloride and 800 mg (9 mmol) of N-ethyl-N-(2-hydroxyethyl1)-amine, 1.07 g (71%) of 2-[2-ethoxy-5-N-ethyl-N-(2-hydroxyethyl)-amino-1-sulphonyl)-phenyl]-5-ethyl-7-cyclopentyl-3 H-imidazo[5,1-f][1,2,4]triazin-4-one are obtained.

R_f=0.31 (dichloromethane/methanol=19:1)

200 MHz ^{1}H-NMR ($CDCl_3$): 1.20 (t, 3H); 1.32 (t, 3H); 1.61 (t, 3H); 1.95 (m, 9H); 2.41 (m, 1H); 3.02 (quart., 2H); 3.35 (m, 4H); 3.65 (m, 1H); 3.80 (m, 2H); 4.33 (quart., 2H); 7.15 (d, 1H); 7.95 (dd, 1H); 8.50 (d, 1H); 9.81 (s, 1H).

EXAMPLE 30

2-[2-Ethoxy-5-(4-(2-hydroxyethyl)-piperazine)-1-sulphonyl)-phenyl]-5-ethyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one



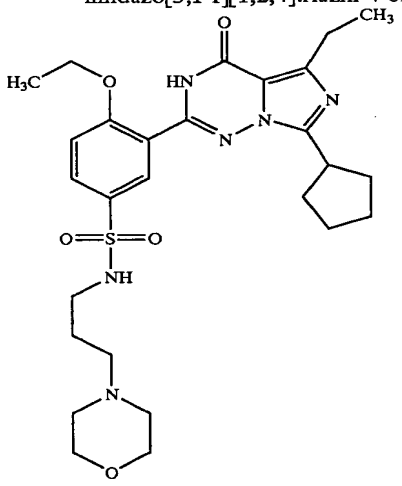
In an analogous manner, starting from 1.35 g (3 mmol) of 3-(7-cyclopentyl-5-ethyl-4-oxo-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxybenzenesulphonyl chloride and 1.17 g (9 mmol) of 4-(2-hydroxyethyl)-piperazine, 1.21 g (74%) of 2-[2-ethoxy-5-(4-(2-hydroxyethyl)-piperazine)-1-sulphonyl)-phenyl]-5-ethyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one are obtained.

R_f=0.21 (dichloromethane/methanol=19:1)

200 MHz ^{1}H-NMR ($CDCl_3$): 1.31 (t, 3H); 1.60 (t, 3H); 1.96 (m, 9H); 2.58 (m, 7H); 3.02 (quart., 2H); 3.10 (m, 4H); 3.61 (m, 3H); 4.35 (quart., 2H); 7.19 (d, 1H); 7.89 (dd, 1H); 8.45 (d, 1H); 9.75 (s, 1H).

EXAMPLE 31

2-[2-Ethoxy-5-(3-(4-morpholino)-propyl)-sulphonamido)-phenyl]-5-ethyl-3H-7-cyclopentyl-imidazo[5,1-f][1,2,4]triazin-4-one



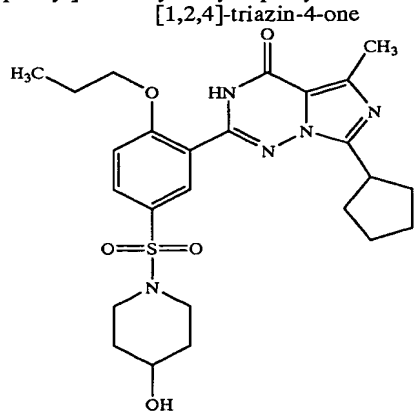
In an analogous manner, starting from 1.35 g (3 mmol) of 3-(7-cyclopentyl-5-ethyl-4-oxo-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxybenzenesulphonyl chloride and 1.30 g (9 mmol) of 4-(3-aminopropyl)-morpholine, 1.44 g (86%) of 2-[2-ethoxy-5-(3-(1-morpholino)-propyl)-sulphonamido)-phenyl]-5-ethyl-7-cyclopentyl-3H-imidazo [5,1-f][1,2,4]triazin-4-one are obtained.

R_f=0.29 (dichloromethane/methanol=19:1)

200 MHz ^{1}H-NMR ($CDCl_3$): 1.31 (t, 3H); 1.60 (t, 3H); 2.02 (m, 12H); 2.46 (m, 8H); 3.02 (quart., 2H); 3.13 (t, 2H); 3.62 (m, 5H); 4.35 (quart., 2H); 7.15 (d, 1H); 7.89 (dd, 1H); 8.55 (d, 1H); 9.82 (s).

EXAMPLE 32

2-[2-Propoxy-5-(4-hydroxypiperidine-1-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



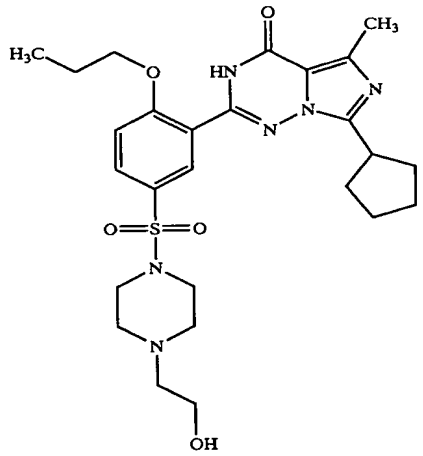
The preparation is carried out analogously to the procedure of Example 1 using 50 mg (0.111 mmol) of 4-propoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 28 mg (0.227 mmol) of 4-hydroxypiperidine. This gives 46 mg (80.5%) of sulphonamide.

R_f=0.53 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 1.05 (t, 3H);1.5–1.6 (m, 2H); 1.65–1.75 (m, 2H); 1.8–2.0 (m, 8H); 1.05–2.2 (m, 2H); 2.6 (s, 3H); 2.8–2.9 (m, 2H); 3.3–3.4 (m, 2H); 3.6–3.7 (m, 2H); 4.15 (t, 2H); 7.35 (d, 1H); 7.9 (dd, 1H); 8.0 (d, 1H).

EXAMPLE 33

2-[2-Propoxy-5-(4-(2-hydroxyethyl)-piperazine-1-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one

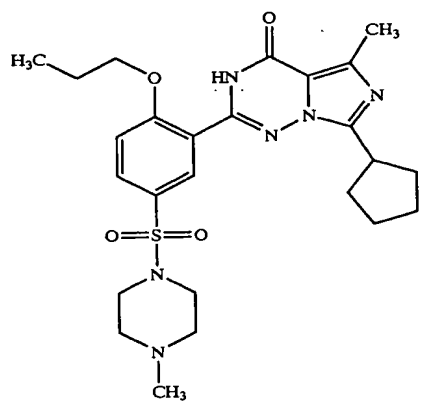


The preparation is carried out analogously to the procedure of Example 1 using 50 mg (0.111 mmol) of 4-propoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 32.4 mg (0.249 mmol) of N-(2-hydroxyethyl)-piperazine. This gives 40 mg (73.6%) of sulphonamide which is purified by recrystallization from ethyl acetate/diethyl ether.

M.p.: 210° C.

EXAMPLE 34

2-[2-Propoxy-5-(4-methylpiperazine-1-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



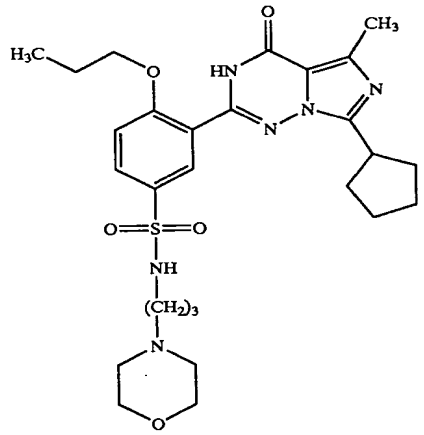
The preparation is carried out analogously to the procedure of Example 1 using 50 mg (0.111 mmol) of 4-propoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 24.9 mg (0.249 mmol) of N-methylpiperazine. This gives 49 mg (95.4%) of sulphonamide.

R_f=0.49 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 1.05 (t, 3H); 1.65–2.2 (m, 2H); 2.3 (s, 3H); 2.45–2.55 (m, 4H); 2.6 (s, 3H); 3.0–3.1 (m, 4H); 3.6 (quin, 1H); 4.2 (t, 2H); 7.4 (d, 1H); 7.95 (dd, 1H); 8.0 (d, 1H).

EXAMPLE 35

2-[2-Propoxy-5-(3-(4-morpholino)-propyl-sulphonamido)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



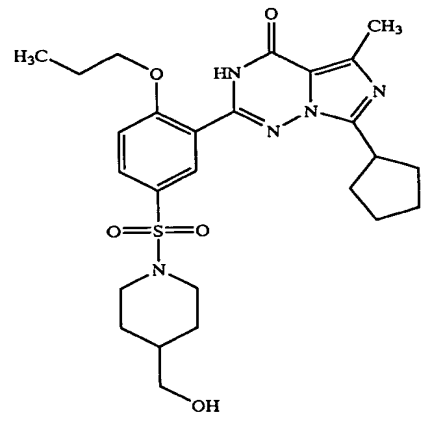
The preparation is carried out analogously to the procedure of Example 1 using 50 mg (0.111 mmol) of 4-propoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 36.7 mg (0.255 mmol) of 3-(4-morpholino)-propylamine. This gives 16 mg (28.1 %) of sulphonamide.

R_f=0.41 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 1.05 (t, 3H); 1.6–2.2 (m, 12H); 2.3–2.45 (m, 6H); 2.6 (s, 3H); 2.95 (t, 2H); 3.6–3.7 (m, 5H); 4.15 (t, 2H); 7.35 (d, ^{1}H); 8.0 (d, 1H); 8.1 (d, 1H).

EXAMPLE 36

2-[2-Propoxy-5-(4-hydroxymethylpiperidine-1-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



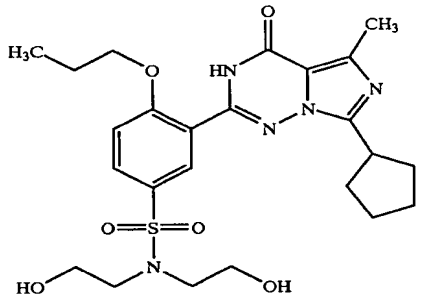
The preparation is carried out analogously to the procedure of Example 1 using 50 mg (0.111 mmol) of 4-propoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 29.3 mg (0.255 mmol) of 4-hydroxymethylpiperidine. This gives 46 mg (85.1%) of sulphonamide.

R_f=0.46 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 1.05 (t, 3H); 1.65–2.0 (m, 13H); 2.05–2.15 (m, 2H); 2.3 (t, 2H); 2.6 (s, 3H); 3.4 (d, 2H); 3.65 (m, ^{1}H); 3.8 (d, 2H); 4.2 (t, 2H); 7.4 (d, 1H); 7.9 (dd, 1H); 8.0 (d, 1H).

EXAMPLE 37

2-[2-Propoxy-5-(N,N-bis-2-hydroxyethyl-sulphonamide)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



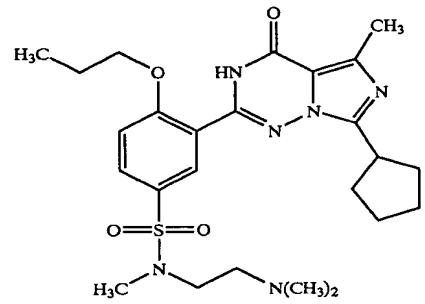
The preparation is carried out analogously to the procedure of Example 1 using 50 mg (0.111 mmol) of 4-propoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 26.8 mg (0.255 mmol) of diethanolamine. This gives 30 mg (56.6%) of sulphonamide.

R_f=0.43 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 1.05 (t, 3H); 1.65–2.2 (m, 10H); 2.6 (s, 3H); 3.3 (m, 4H); 3.65 (quin, 1H); 3.7 (t, 4H); 4.2 (t, 2H); 7.35 (d, 1H); 8.0 (dd, 1H); 8.1 (d, 1H).

EXAMPLE 38

2-[2-Propoxy-5-(N-methyl-N-(2-dimethylaminoethyl)-sulphonamido)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



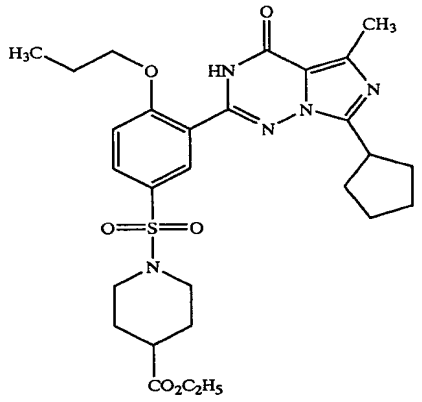
The preparation is carried out analogously to the procedure of Example 1 using 50 mg (0.111 mmol) of 4-propoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 26 mg (0.255 mmol) of N-methyl-N-(2-dimethylaminoethyl)-amine. This gives 26 mg (49.3%) of sulphonamide.

R_f=0.3 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 1.05 (t, 3H); ,165–2.2 (m, 10H); 2.3 (s, 6H); 2.55 (t, 2H); 2.6 (s, 3H); 2.8 (s, 3h); 3.15 (t, 2H); 3.65 (quin., 1H); 4.2 (t, 2H); 7.4 (d, 1H); 7.95 (dd, 1H); 8.05 (d, 1H).

EXAMPLE 39

2-[2-Propoxy-5-(4-ethoxycarbonylpiperidine-1-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one

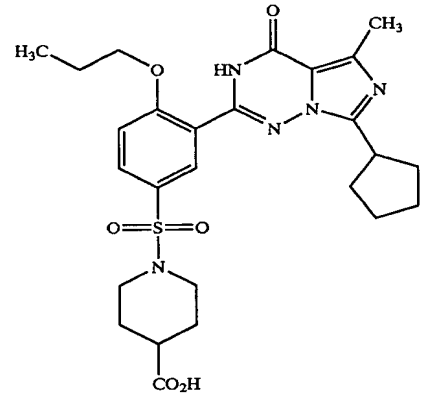


The preparation is carried out analogously to the procedure of Example 1 using 50 mg (0.111 mmol) of 4-propoxy-3-(5-methyl-4-oxo-7-cyclopentyl-3,4-dihydro[5,1-f][1,2,4] triazin-2-yl)-benzenesulphonyl chloride and 48.7 mg (0.31 mmol) of ethyl 4-piperidinecarboxylate. This gives 80 mg (90.1 %) of sulphonamide.

^{1}H-NMR (CD_3OD): 1.05 (t, 2H); 1.2 (t, 2H); 1.65–2.0 (m, 12H); 2.15–2.35 (m, 3H); 2.6 (td, 2H); 2.7 (s, 3H); 3.5–3.6 (, 2H); 3.75 (quin., 1H); 4.1 (quar., 2H); 4.2 (quar., 2H); 7.4 (d, 1H); 7.95 dd, 1H); 8.05 (d, 1H).

EXAMPLE 40

2-[2-Propoxy-5-(4-carboxypiperidine-1-sulphonyl)-phenyl]-5-methyl-7-cyclopentyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



80 mg (0.14 mmol) of the ester from Example 39 are stirred at room temperature in a mixture of 5 ml of methanol and 1 ml of 4 n NaOH for 30 minutes. 10 ml of dichloromethane are added, the mixture is extracted with 10 ml of 2 n HCl solution and the organic phase is separated off, dried over sodium sulphate and evaporated. The residue is recrystallized from diethyl ether.

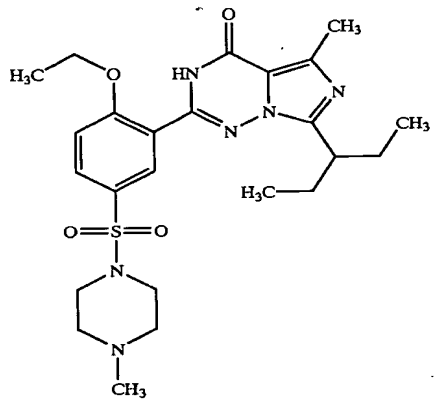
Yield: 50 mg (65.7%)

R_f=0.47 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 1.05 (t, 3H); 1.65–2.0 (m, 12H); 2.2–2.35 (m, 3h); 2.6 (td, 2H); 2.7 (s, 3H); 3.55–3.6 (m, 2H); 3.75 (quin., 1H); 4.2 (t, 2H); 7.4 (d, 1H); 7.95 (dd, 1H); 8.05 (d, 1H).

EXAMPLE 41

2-[2-Ethoxy-5-(4-methylpiperazine-1-sulphonyl)-phenyl]-7-(1-ethylpropyl)-5-methyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one



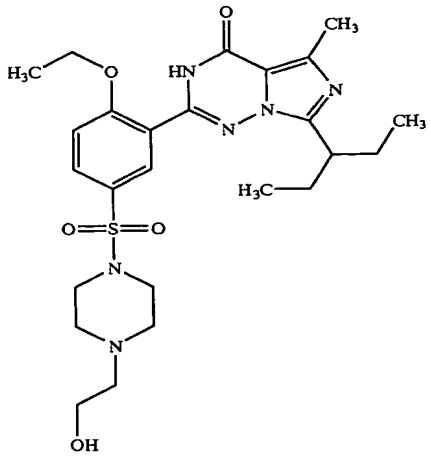
50 mg (0.114 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-(1-ethylpropyl)-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride are initially charged in 5 ml of dichloromethane and a spatula tip of 4 dimethylaminopyridine is added, followed by 30 mg (0.342 mmol) of N-methylpiperazine. The mixture is stirred at room temperature overnight, diluted with dichloromethane, washed twice with saturated ammonium chloride solution, dried over sodium sulphate, concentrated and filtered through silica gel (methanol).

Yield: 45 mg (78.6% of theory)

200 MHz ^{1}H-NMR ($CDCl_3$): 0.85 (t, 6H); 1.63 (t, 3H); 1.85 (m, 4H); 2.39 (s, 3H); 2.65 (m, 7H); 3.17 (m, 5H); 4.35 (q, 2H); 7.18 (d, 1H); 7.88 (dd, 1H); 8.49 (d, 1H); 9.64 (bs, 1H).

EXAMPLE 42

2-[2-Ethoxy-5-(4-(2-hydroxyethyl)-piperazine-1-sulphonyl)-phenyl]-7-(1-ethylpropyl)-5-methyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one

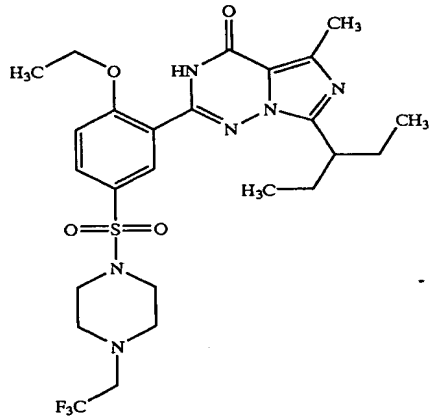


Analogously, using 100 mg (0.221 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-(1-ethylpropyl)-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride and 90 mg (0.662 mmol) of N-(2-hydroxyethyl)-piperazine, 99 mg (84.2% of theory) of 2-[2-ethoxy-5-(4-(2-hydroxyethyl)-piperazine-1-sulphonyl)-phenyl]-7-(1-ethylpropyl)-5-methyl-3H-imidazo[5,1-f]-[1,2,4]triazin-4-one are obtained.

200 MHz ^{1}H-NMR ($CDCl_3$): 0.87 (t, 6H); 1.62 (t, 3H); 1.84 (m, 4H); 2.56–2.74 (m, 9H); 3.08–3.32 (m, 5H); 3.63 (t, 2H); 4.37 (q, 2H); 7.18 (d, 1H); 7.9 (dd, 1H); 8.5 (d, 1H); 9.67 (bs, 1H).

EXAMPLE 43

2-[2-Ethoxy-5-(4-(2,2,2-trifluoroethyl)-piperazine-1-sulphonyl)-phenyl]-7-(1-ethylpropyl)-5-methyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one



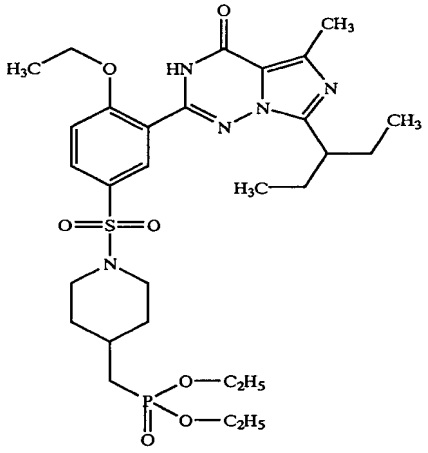
Analogously, using 100 mg (0.228 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-(1-ethylpropyl)-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride and 120 mg (0.69 mmol) of (2,2,2-trifluoroethyl)-piperazine, 72 mg

(18.2% of theory) of 2-[2-ethoxy-5-(4-(2,2,2-trifluoroethyl)-piperazine-1-sulphonyl)-phenyl]-7-(1-ethylpropyl)-5-methyl-3H-imidazo-[5,1-f][1,2,4]triazin-4-one are obtained.

200 MHz ^{1}H-NMR ($CDCl_3$): 0.87 (t, 6H); 1.63 (t, 3H); 1.89 (m, 4H); 2.71 (s, 3H); 2.8 (m, 4H); 2.97 (q, 2H); 3.1 (m, 4H); 3.25 (m, 1H); 4.38 (q, 2H); 7.19 (s, 1H); 7.89 (dd, 1H); 8.49 (d, 1H); 9.71 (bs, 1H).

EXAMPLE 44

2-[2-Ethoxy-5-(1-(4-diethoxyphosphonylmethylpiperidinyl)-sulphonyl)-phenyl]-7-(1-ethylpropyl)-5-methyl-3H-imid-azo[5,1-f]-[1,2,4]-triazin-4-one

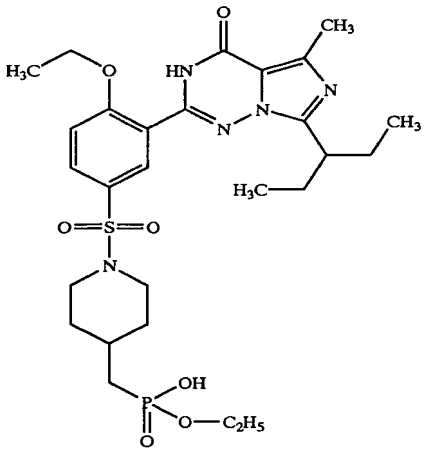


Analogously, using 100 mg (0.228 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-(1-ethylpropyl)-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride and 161 mg (0.683 mmol) of 4-diethoxyphosphonylmethyl-piperidine, 96.2 mg (66.2% of theory) of 2-[2-ethoxy-5-(1-(4-diethoxyphosphonylmethylpiperidine)-sulphonyl)-phenyl]-7-(1-ethylpropyl)-5-methyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one are obtained.

200 MHz ^{1}H-NMR ($CDCl_3$): 0.86 (t, 6H); 1.3 (t, 6H); 1.38–2.02 (m, 14H); 2.35 (dt, 2H); 2.68 (s, 3H); 3.23 (m, 1H); 3.8 (d, 2H); 4.08 (m, 4H); 4.36 (q, 2H); 7.17 (d, 1h); 7.88 (dd, 1H); 8.49 (d, 1H); 9.7 (bs, 1H).

EXAMPLE 45

2-[2-Ethoxy-5-(1-(4-monoethoxyphosphonylmethylpiperidinyl)-sulphonyl)-phenyl]-7-(1-ethylpropyl)-5-methyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one

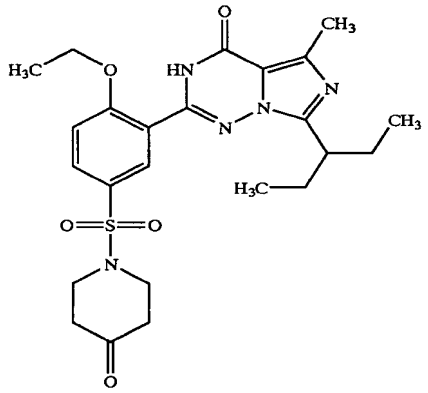


61.4 mg (96.2 μmol) of 2-[2-ethoxy-5-(1-(4-diethoxyphosphonylmethylpiperidinyl)-sulphonyl)-phenyl]-7-(1-ethylpropyl)-5-methyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one are heated under reflux with 21.6 mg (0.385 mmol) of KOH powder in 5 ml of ethanol overnight. The mixture is concentrated, taken up in water, acidified with 1N hydrochloric acid and extracted three times with dichloromethane. The extracts are dried and concentrated.

Yield: 42 mg (71.6% of theory)

EXAMPLE 46

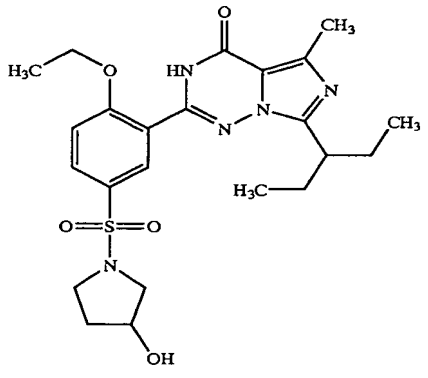
2-[2-Ethoxy-5-(4-oxopiperidine-1-sulphonyl)-phenyl]-7-(1-ethylpropyl)-5-methyl-3H-imid-azo[5,1-f][1,2,4]triazin-4-one



Analogously using 300 mg (0.683 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-(1-ethylpropyl)-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride and 310 mg (2.05 mmol) of 4,4-dihydroxipiperidine hydrochloride, 18 mg (5.2% of theory) of 2-[2-ethoxy-5-(4-oxopiperidine-1-sulphonyl)-phenyl]-7-(1-ethylpropyl)-5-methyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one are obtained.

EXAMPLE 47

2-[2-Ethoxy-5-(3-hydroxypyrrolidine-1-sulphonyl)-phenyl]-7-(1-ethylpropyl)-5-methyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one

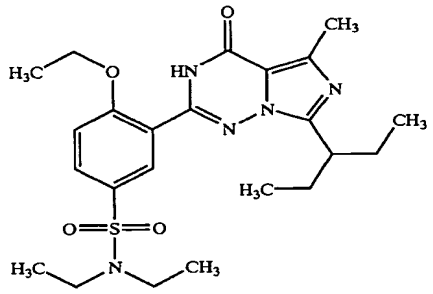


Analogously, using 100 mg (0.228 mmol) of 4-ethoxy-3-(5-methyl4-oxo-7-(1-ethylpropyl)-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride and 60 mg (0.683 mmol) of 3-hydroxypyrrolidine, 55 mg (49.1% of theory) of 2-[2-ethoxy-5-(3-hydroxy-pyrrolidine-1-sulphonyl)-phenyl]-7-(1-ethylpropyl)-5-methyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one are obtained.

200 MHz ^{1}H-NMR ($CDCl_3$): 0.85 (t, 6H); 1.61 (t, 3H); 1.72–2.1 (m, 7H); 2.69 (s, 3H); 3.22–3.55 (m, 5H); 4.35 (q, 2H); 4.45 (m, 1H); 7.18 (d, 1H); 7.99 (dd, 1H); 8.57 (d, 1H); 9.8 (bs, 1H).

EXAMPLE 48

2-[2-Ethoxy-5-(N,N-diethyl-sulphonamido)-phenyl]-5-methyl-7-(1-ethylpropyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one

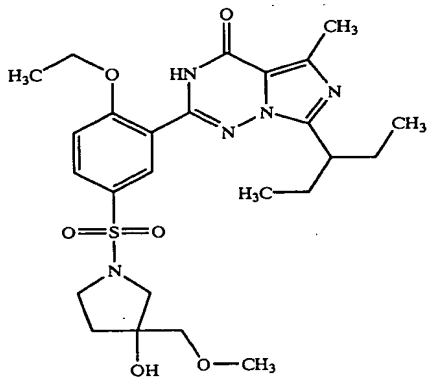


Analogously, using 100 mg (0.228 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-(1-ethylpropyl)-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride and 50 mg (0.683 mmol) of diethylamine, 78 mg (72.3% of theory) of 2-[2-ethoxy-5-(N,N-diethyl-sulphonamido)-phenyl]-5-methyl-7-(1-ethylpropyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one are obtained.

200 MHz ^{1}H-NMR ($CDCl_3$): 0.87 (t, 6H); 1.2 (t, 6H); 1.62 (t, 3H); 1.88 (m, 4H); 2.69 (s, 3H); 3.3 (m, 5H); 4.35 (q, 2H); 7.14 (d, 1H); 7.96 (dd, 1H); 8.57 (d, 1H); 9.78 (bs, 1H).

EXAMPLE 49

2-[2-Ethoxy-5-(3-hydroxy-3-methoxymethylpyrrolidine-1-sulphonyl)-phenyl]-7-(1-ethylpropyl)-5-methyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one

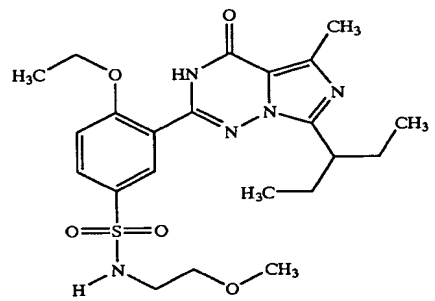


Analogously, using 100 mg (0.228 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-(1-ethylpropyl)-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride and 90 mg (0.683 mmol) of 3-hydroxy-3-methoxymethyl-pyrrolidine, 89 mg (72.9% of theory) of 2-[2-ethoxy-5-(3-hydroxy-3-methoxymethylpyrrolidine-1-sulphonyl)-phenyl]-7-(1-ethylpropyl)-5-methyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one are obtained.

200 MHz ^{1}H-NMR ($CDCl_3$): 0.88 (t, 6H); 1.62 (t, 3H); 1.72–2.08 (m, 6H); 2.47 (s, 1H); 2.7 (s, 3H); 3.13–3.63 (m, 10H); 4.36 (q, 2H); 7.17 (d, 1H); 7.98 (dd, 1H); 8.57 d, 1H); 9.78 (bs, 1H).

EXAMPLE 50

2-[2-Ethoxy-5-(N-2-methoxyethyl-sulphonamido)-phenyl]-5-methyl-7-(1-ethylpropyl)-3H-imidazo[5,1-f][1,2,4]-triazin-4-one

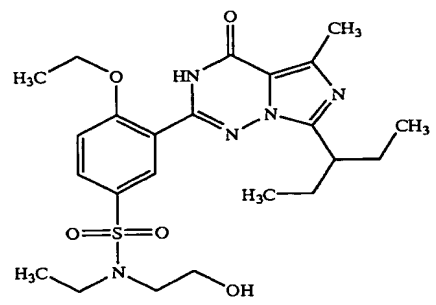


Analogously, using 350 mg (0.797 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-(1-ethylpropyl)-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride and 180 mg (2.392 mmol) of methoxyethylamine, 251 mg (66% of theory) of 2-[2-ethoxy-5-(N-2-methoxyethyl-sulphonamide)-phenyl]-5-methyl-7-(1-ethylpropyl)-3H-imidazo[5,1-f][1,2,4]-triazin-4-one are obtained.

200 MHz ^{1}H-NMR (DMSO-d_6): 0.75 (t, 6H); 1.32 (t, 3H); 1.61–1.72 (m, 4H); 2.93 (q, 2H); 3.1 (m, 1H); 3.18 (s, 3H); 3.26–3.4 (m, 5H); 4.19 (q, 2H); 7.35 (d, 1H); 7.76 t, 1H); 7.86–7.96 (m, 2H); 11.7 (bs, 1H).

EXAMPLE 51

2-[2-Ethoxy-5-(N-ethyl-N-(2-hydroxyethyl)-sulphonamido)-phenyl]-5-methyl-7-(1-ethylpropyl)-3H-imidazo[5,1-f][1,2,4]-triazin-4-one

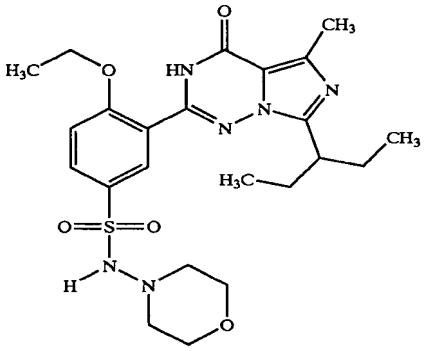


Analogously, using 400 mg (0.911 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-(1-ethylpropyl)-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride and 240 mg (2.734 mmol) of 2-(ethylamino)-ethanol, 261 mg (58.3% of theory) of 2-[2-ethoxy-5-(N-2-ethyl-N-(2-hydroxyethyl)-sulphonamide)-phenyl]-5-methyl-7-(1-ethylpropyl)-3H-imidazo[5,1-f][1,2,4]-triazin-4-one are obtained.

200 MHz ^{1}H-NMR (DMSO-d_6):0.78 (t, 6H); 1.08 (t, 3H); 1.33 (t, 3H); 1.6–1.88 (m, 4H); 2.99–3.28 (m, 7H); 3.38 (m, 1H); 3.52 (q, 2H); 4.2 (q, 2H); 4.81 (t, 1H); 7.34 (d, 1H); 7.86–8.0 (m, 2H); 11.69 (bs, 1H).

EXAMPLE 52

2-[2-Ethoxy-5-(N-(4-morpholinyl)sulphonamido)-phenyl]-5-methyl-7-(1-ethylpropyl)-3H-imidazo[5,1-f][1,2,4]-triazin-4-one

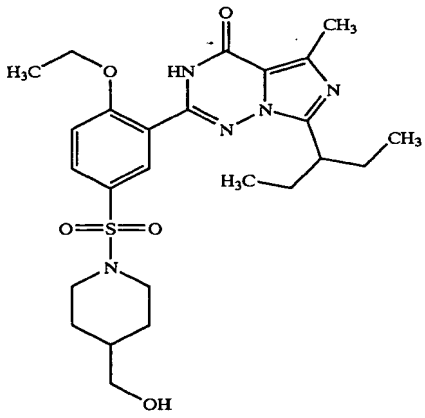


Analogously, using 400 mg (0.911 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-(1-ethylpropyl)-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride and 280 mg (2.734 mmol) of 4-aminomorpholine, 109 mg (21.1% of theory) of 2-[2-ethoxy-5-(N-(4-morpholinyl) sulphonamido)-phenyl]-5-methyl-7-(1-ethylpropyl)-3H-imidazo[5,1-f][1,2,4]-triazin-4-one are obtained.

200 MHz ^{1}H-NMR ($CDCl_3$): 0.88 (t, 6H); 1.63 (t, 3H); 1.85–2.28 (m, 4H); 2.88 (s, 3H); 3.05 (m, 4H); 3.45 (m, 1H); 3.76 (m, 4H); 4.42 (q, 2H); 7.2–7.35 (m, 2H); 7.96 (m, 1H); 8.45 (m, 1H); 10.23 (bs, 1H).

EXAMPLE 53

2-[2-Ethoxy-5-(4-hydroxymethylpiperidine-1-sulphonyl)-phenyl]-7-(1-ethylpropyl)-5-methyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one

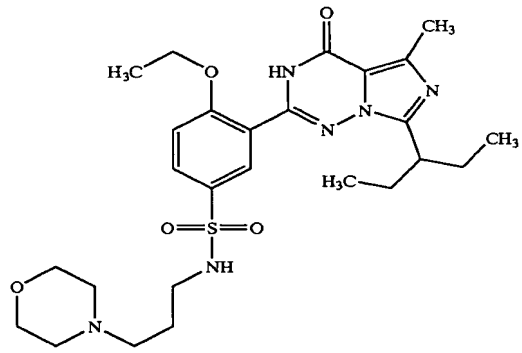


Analogously, using 400 mg (0.911 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-(1-ethylpropyl)-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride and 310 mg (2.734 mmol) of 4-hydroxymethylpiperidine, 270 mg (57.3% of theory) of 2-[2-ethoxy-5-(4-hydroxy-methylpiperidine-1-sulphonyl)-phenyl]-7-(1-ethylpropyl)-5-methyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one.

200 MHz ^{1}H-NMR (DMSO-d_6): 0.77 (t, 6H); 1.05–1.43 (m, 6H); 1.58–1.85 (m, 6H); 2.12–2.38 (m, 2H); 2.52 (s, 3H); 3.08 (m, 1H); 3.22 (t, 2H); 3.55–3.72 (m, 2H); 4.2 (q, 2H); 4.51 (t, 1H); 7.38 (d, 1H); 7.78–7.92 (m, 2H); 11.7 (bs, 1H).

EXAMPLE 54

2-[2-Ethoxy-5-(3-(1-morpholino)-propyl)-sulphonamido)-phenyl]-5-methyl-7-(1-ethylpropyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one



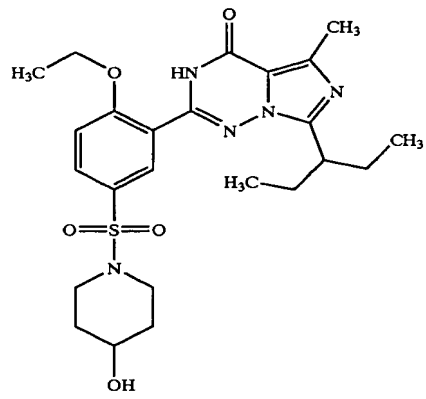
In an analogous manner, starting from 0.44 g (1 mmol) of 3-(1-ethylpropyl)-5-methyl-4-oxo-3,4-dihydroimidazo[5,1-f][1,2,4]triazin-2-yl)4-ethoxy-benzenesulphonyl chloride and 0.43 g (3 mmol) of 4-(3-aminopropyl)-morpholine 0.45 g (81%) of 2-[2-ethoxy-5-(3-(1-morpholino)-propyl)-sulphonamido)-phenyl]-5-methyl-7-(1-ethylpropyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one are obtained.

R_f=0.18 (dichloromethane/methanol=19:1)

200 MHz ^{1}H-NMR ($CDCl_3$): 1.31 (t, 3H); 1.61 (t, 3H); 1.87 (m, 14H); 2.66 (s, 3H); 3.00 (m 2H); 3.28 (m, 3H); 3.85 (m, 1H); 4.35 (quart., 2H); 7.17 (d, 1H); 7.90 (dd, 1H); 8.50 (d, 1H); 9.72 (s, 1H).

EXAMPLE 55

2-[2-Ethoxy-5-(4-hydroxypiperidine-1-sulphonyl)-phenyl]-5-methyl-7-(1-ethylpropyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one

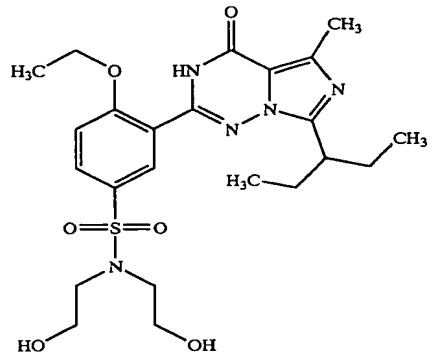


In an analogous manner, starting from 0.44 g (1 mmol) of 3-(7-(1-ethylpropyl)-5-methyl-4-oxo-3,4-dihydroimidazo [5,1-f][1,2,4]triazin-2-yl)-4-ethoxy-benzenesulphonyl chloride and 0.30 g (3 mmol) of 4-hydroxypiperidine, 0.33 g (65%) of 2-[2-ethoxy-5-(4-hydroxypiperidine-1-sulphonyl)-phenyl]-5-methyl-7-(1-ethylpropyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one are obtained.

R_f=0.25 (dichloromethane/methanol=19:1)

EXAMPLE 56

2-[2-Ethoxy-5-(bishydroxyethylamino-1-sulphonyl)-phenyl]-5-methyl-7-(1-ethylpropyl)-3H-imidazo-[5,1-f][1,2,4]triazin-4-one



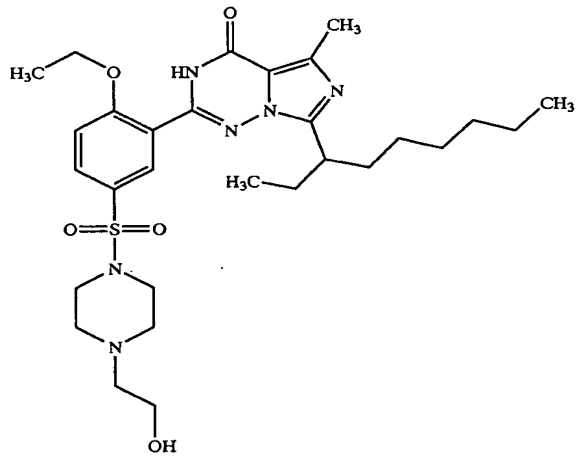
In an analogous manner, starting from 0.3 g (0.68 mmol) of 3-(7-(1-ethylpropyl)-5-ethyl-4-oxo-3,4-dihydroimidazo [5,1-f][1,2,4]triazin-2-yl)-4-ethoxy-benzenesulphonyl chloride and 0.22 g (2.01 mmol) of diethanolamine, 0.147 g (42%) of 2-[2-ethoxy-5-(bishydroxyethylamino-1-sulphonyl)-phenyl]-5-methyl-7-(1-ethylpropyl)-3H-imidazo-[5,1-f][1,2,4]triazin-4-one are obtained.

R_f=0.57 (dichloromethane/methanol=9:1)

200 MHz ^{1}H-NMR ($CDCl_3$): 0.98 (t, 6H); 1.62 (t, 3H); 1.89 (m, 4H); 2.67 (s, 3H); 3.23 (m, 3H); 3.36 (t, 4H); 3.90 (t, 4H); 4.36 (quart., 2H); 7.18 (d, 1H); 7.96 (dd, 1H); 8.55 (d, 1H); 9.68 (s, 1H).

EXAMPLE 57

2-[2-Ethoxy-5-(4-(2-hydroxyethyl)-piperazine-1-sulphonyl)-phenyl]-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one



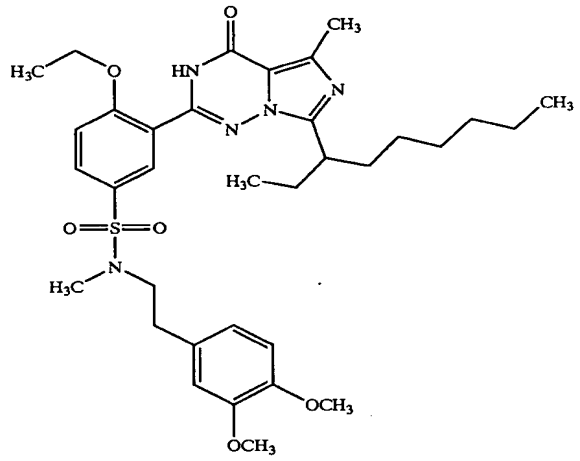
The preparation is carried out analogously to the procedure of Example 1 using 500 mg (1.01 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-(2-ethylheptyl)-3,4-dihydro[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 290 mg (2.2 mmol) of 4-(2-hydroxyethyl)-piperazine. This gives 170 mg (28.6%) of sulphonamide.

R_f=0.56 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 0.75–0.85 (2t, 6H); 1.1–1.35 (m, 8H); 1.45 (t, 3H); 1.65–1.95 (m, 4H); 2.0 (t, 2H); 2.55–2.65 (m, 7H); 3.0–3.1 (m, 4H); 3.3 (quin., 1H); 3.6 (t, 2H); 4.3 (quar., 2H); 7.4 (d, 1H); 7.95 (dd,, 1H); 8.0 (d, 1H).

EXAMPLE 58

2-[2-Ethoxy-5-(N-methyl-N-(2-(3,4-dimethoxyphenyl)-ethyl)sulphonamido-phenyl]-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f][1,2,4] triazin-4-one



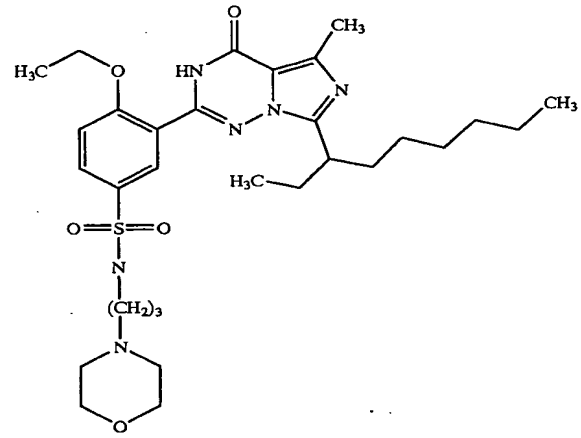
The preparation is carried out analogously to the procedure of Example 1 using 500 mg (1.01 mol) of 4-ethoxy-3-(5-methyl-4-oxo-7-(2-ethylheptyl)-3,4-dihydro[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 433 mg (2.2 mmol) of N-methyl-N-2-(3,4-dimethoxyphenyl)-ethylamine. This gives 153 mg (23.2%) of sulphonamide.

R_f=0.78 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 0.7–0.5 (t, 6H); 1.0–1.35 (m, 8H); 1.45 (t, 2H); 1.6–1.95 (m, 4H); 2.6 (s, 3h); 2.75 (s, 3H); 2.8 (t, 2H); 3.15–3.35 (m, 3H); 3.75 (s, 6H); 4.3 (quar. 2H); 6.7–6.85 (m, 3H); 7.3 (d, 1H); 7.9 (dd, 1H); 8.0 (d, 1H).

EXAMPLE 59

2-[2-Ethoxy-5-(3-(4-morpholino)-propyl-sulphonamido)-phenyl]-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one



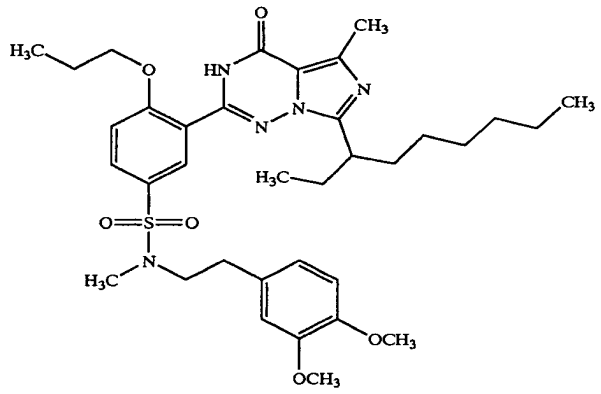
The preparation is carried out analogously to the procedure of Example 1 using 500 mg (1.01 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-(2-ethylheptyl)-3,4-dihydro[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 320 mg (2.2 mmol) of 3-(4-morpholino)-propylamine. This gives 175 mg (28.7%) of sulphonamide.

R_f=0.58 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 0.5–0.9 (t, 6H);1.1–1.35 (m, 8H); 1.45 (t, 3H); 1.65 (quin., 2H); 1.7–1.9 (m, 4H); 2.3–2.45 (m, 6h); 2.6 (s, 3H); 2.95 (t, 2H); 3.3 (m, 1H); 3.665 (2t, 4H); 4.3 (quar., 2h); 7.35 (d, 1H); 8.0 (dd, 1H); 8. 1(D, 1H).

EXAMPLE 60

2-[2-Propoxy-5-(N-methyl-N(2-(3,4-dimethoxyphenyl)-ethyl)-sulphonamido)-phenyl]-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f][1,2,4] triazin-4-one



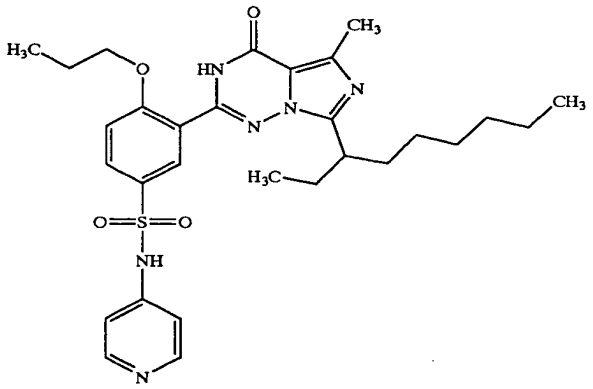
The preparation is carried out analogously to the procedure of Example 1 using 50 mg (0.1 mmol) of 4-propoxy-3-(5-methyl-4-oxo-7-(2-ethylheptyl)-3,4-dihydro[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 50mg (0.25 mmol) of N-methyl-N-2-(3,4-dimethoxyphenyl)-ethylamine. This gives 45 mg (66%) of sulphonamide.

R_f=0.74 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 0.75 (t, 3H); 0.8 (t, 3h); 105 (t, 3H); 10–1.3 (m, 8H); 1.6–1.9 (m, 6h); 2.6 (s, 3H); 2.8 (s, 3H); 2.85 (t, 2H); 3.2–3.4 (m, 3H); 3.8 (s, 6H); 4.2 (t, 2H); 6.7–6.85 (m, 3H); 7.3 (d, 1H); 7.9 (dd, 1H); 8.0 (d, 1H).

EXAMPLE 61

2-[2-Propoxy-5-(4-pyridyl-sulphonamido)-phenyl]-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f][1,2,4] triazin-4-one

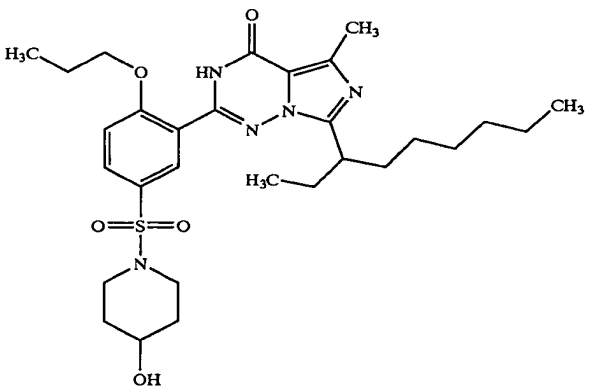


The preparation is carried out analogously to the procedure of Example 1 using 100 mg (0.196 mmol) of 4-propoxy-3-(5-methyl-4-oxo-7-(2-ethylheptyl)-3,4-dihydro[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 22 mg (0.236 mmol) of 4-aminopyridine in the presence of 40 mg (0.4 mmol) of triethylamine. This gives 35 mg (31.4%) of sulphonamide which can be recrystallized from ethyl acetate/diethyl ether.

^{1}H-NMR (CD_3OD): 0.8 (2t, 6h); 1.0 (t, 3H); 1.05–1.35 (m, 8); 1.7–1.9 (m, 6H); 2.6 s, 3H); 3.35 (m, 1H); 4.15 (t,, 2H); 7.1 (d, 1h); 7.3 (d, 1H); 8.0 (m, 2H); 8.05 (dd, 1H); 8.1 (d, 1H).

EXAMPLE 62

2-[2-Propoxy-5-(4-hydroxypiperidine-1-sulphonyl)-phenyl]-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one



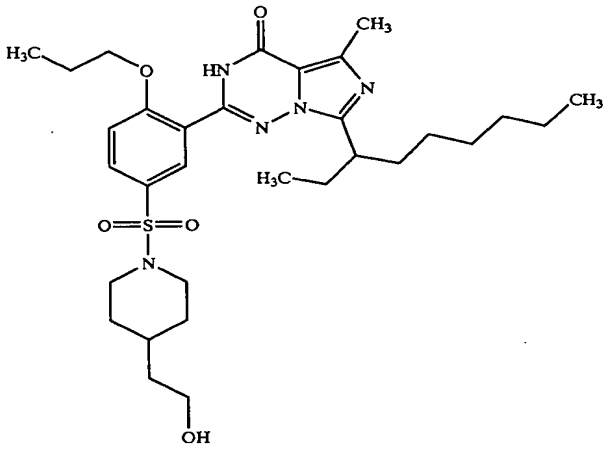
The preparation is carried out analogously to the procedure of Example 1 using 50 mg (0.1 mmol) of 4-propoxy-3-(5-methyl-4-oxo-7-(2-ethylheptyl)-3,4-dihydro[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 20 mg (0.2 mmol) of 4-hydroxypiperidine. This gives 43 mg (76.3%) of sulphonamide.

R_f=0.51 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR ($CDCl_3$): 0.7–0.85 (m, 6H). 1.05–1.3 (m, 11H); 135–2.05 (m, 14H); 2.56 (s, 3H);. 2.85–3.0 (m, 2H); 3.15–3.35 (m, 3H); 3.6–3.7 (m, 1H); 4.2 (t, 2H); 7.1 (d, 1h); 7.85 (dd, 1H); 7.95 (d, 1H); 9.8 (broad, 1H).

EXAMPLE 63

2-[2-Propoxy-5-(4-(2-hydroxyethyl)-piperazine-1-sulphonyl)-phenyl]-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one



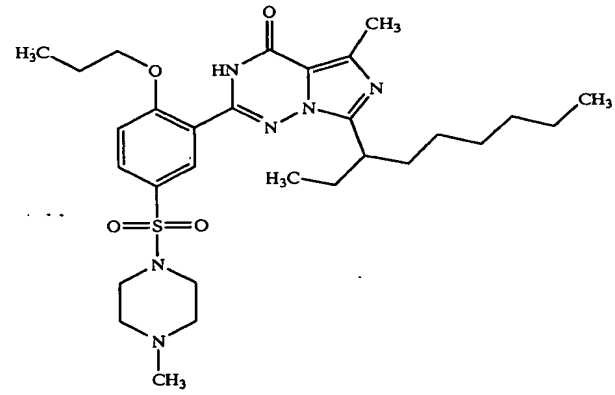
The preparation is carried out analogously to the procedure of Example 1 using 50 mg (0.1 mmol) of 4-propoxy-3-(5-methyl-4-oxo-7-(2-ethylheptyl)-3,4-dihydro[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 26 mg (0.2 mmol) of N-(2-hydroxy-ethyl)-piperazine. This gives 13 mg (22%) of sulphonamide.

R_f=0.46 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR ($CDCl_3$): 0.7–0.85 (m, 6H); 1.0–1.3 (m, 11H); 1.6–2.0 (m, 6H); 2.55 (s, 3H); 2.5–2.7 (m, 4H); 3.0–3.1 (m, 3H); 3.15–3.3 (m, 1H); 3.6 (t, 2H); 4.2 (t, 2H); 7.15 (d, 1H); 7.7 (dd, 1H); 7.9 (d, 1H); 9.7 (broad, 1H).

EXAMPLE 64

2-[2-Propoxy-5-(4-methylpiperazine-1-sulphonyl)-phenyl]-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one



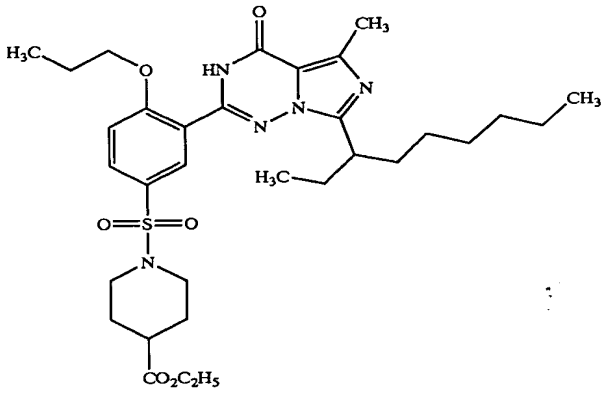
The preparation is carried out analogously to the procedure of Example 1 using 50 mg (0.1 mmol) of 4-propoxy-3-(5-methyl-4-oxo-7-(2-ethylheptyl)-3,4-dihydro[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 20 mg (0.2 mmol) of N-methyl-piperazine. This gives 42 mg (74.7%) of sulphonamide.

R_f=0.46 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR ($CDCl_3$): 0.75–0.9 (m, 6H); 1.1–1.35 (m, 11H); 1.6–2.1 (m, 10H); 2.4 (s, 3H); 2.65 (s, 3H); 2.6–2.75 (m, 2H); 3.1–3.4 (m, 4H); 4.25 (t, 2H); 7.9 (d, 1H); 8.5 (d, 1H). 9.7 (broad, 1H):

EXAMPLE 65

2-[2-Propoxy-5-(4-ethoxycarbonylpiperidine-1-sulphonyl)-phenyl]-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one

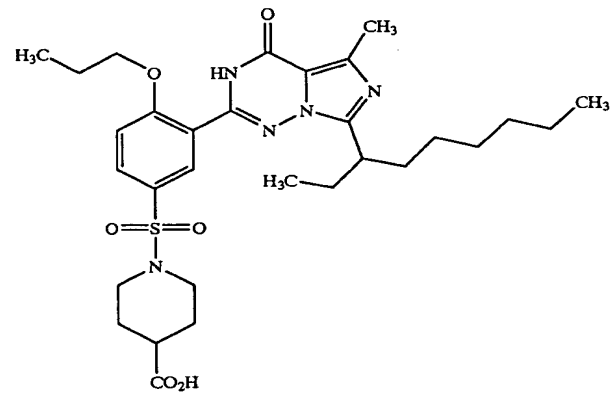


The preparation is carried out analogously to the procedure of Example 1 using 70 mg (0.138 mmol) of 4-propoxy-3-(5-methyl-4-oxo-7-(2-ethylheptyl)-3,4-dihydro[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 43 mg of ethyl piperidinecarboxylate. This gives 55 mg (63.5%) of sulphonamide.

^{1}H-NMR (CD_3OD): 0.85 (t, 3H); 0.9 (t, 3H); 1.1 (t, 3H); 1.2 (t, 3H); 1.2–1.4 (m, 8H); 1.65–2.05 (m, 10H); 2.3 (m, 1H); 2.6 (td, 2H); 2.75 (s, 3H); 3.5 (quin., 1H); 3.6 (m, 2H); 4.1 (quar., 2H); 4.2 (t, 2H); 7.4 (d, 1H); 7.95–8.05 (m, 2H):

EXAMPLE 66

2-[2-Propoxy-5-(4-carboxypiperidine-1-sulphonyl)-phenyl]-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one



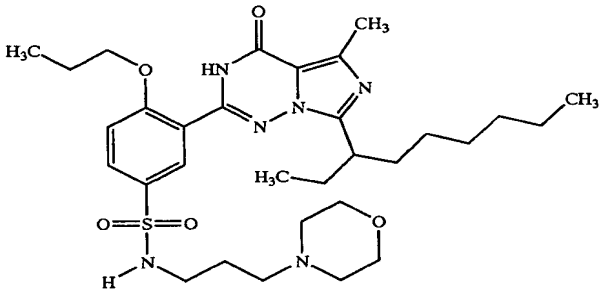
62 mg (0.098 mmol) of the ester from Example 65 are stirred at room temperature in 6 ml of 4 n $NaOH/H_2O$ (1:5) for 30 minutes. 20 ml of dichloromethane are added, the mixture is extracted with 2 n HCl solution, the organic phase is dried with sodium sulphate and the solvent is removed under reduced pressure.

R_f=0.44 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 0.85 (t, 3H); 0.9 (t, 3H); 1.05 (t, 3H); 1.2–1.4 (m, 8H); 1.7–2.05 (m, 10H); 2.75–2.9 (m, 1H); 2.6 (td, 2H); 2.75 (s, 3H); 3.5 (quin., 1H); 3.55–3.65 (m, 2H); 4.2 (t, 2H); 7.4 (d, 1H); 7.95–8.0 (m, 2H).

EXAMPLE 67

2-[2-Propoxy-5-(3-(4-morpholino)-propyl)-sulphonamido)-phenyl]-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one



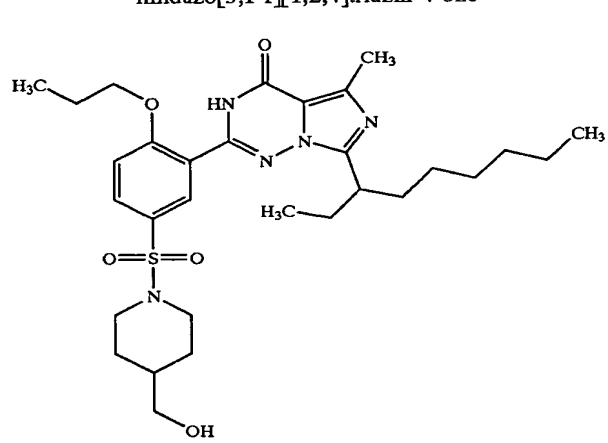
The preparation is carried out analogously to the procedure of Example 1 using 52 mg (0.102 mmol) of 4-propoxy-3-(5-methyl -oxo-7-(2-ethylheptyl)-3,4-dihydro[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 37 mg (0.255 mmol) of 3-(4-morpholino)-propylamine. This gives 45 mg (71.4% of sulphonamide.

R_f=0.41 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 0.75–0.95 (m, 6H); 1.05 (t, 3H); 1.05–1.35 (m, 8H); 1.65 (t, 2H); 1.6–1.95 (m, 6H); 2.3–2.45 (m, 6H); 2.6 (s, 3H); 2.95 (t, 2H); 3.25 (m, 1H); 3.6–3.7 m, 4H); 4.2 (t, 2H); 7.35 (d, 1H); 8.0 (dd, 1H); 8.1 (d, 1H).

EXAMPLE 68

2-[2-Propoxy-5-(4-hydroxymethylpiperidine-1-sulphonyl)-phenyl]-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one



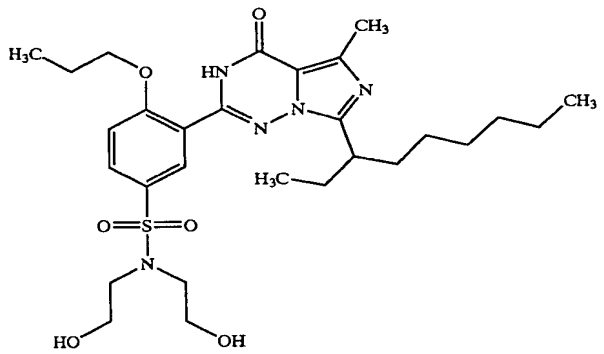
The preparation is carried out analogously to the procedure of Example 1 using 52 mg (0.102 mmol) of 4-propoxy-3-(5-methyl-,4-oxo-7-(2-ethylheptyl)-3,4-dihydro[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 29.3 mg (0.255 mmol) of 4-hydroxymethylpiperidine. This gives 45 mg (74.9%) of sulphonamide.

R_f=0.44 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 0.75–0.9 (m, 6H); 1.05 (t, 3H); 1.0–1.45 (m, 10H); 1.7–1.95 (m, 8H); 2.35 (t, 2H; 2.6 (s, 3H); 3.2–3.4 (m, 2H); 3.8 (d, 2H); 4.2 (t, 2H); 7.4 (d, 1H); 7.9–8.0 (m, 2H).

EXAMPLE 69

2-[2-Propoxy-5-(N,N-bis-2-hydroxyethyl-sulphonamido)-phenyl]-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f][1,2,4]triazin-4-one



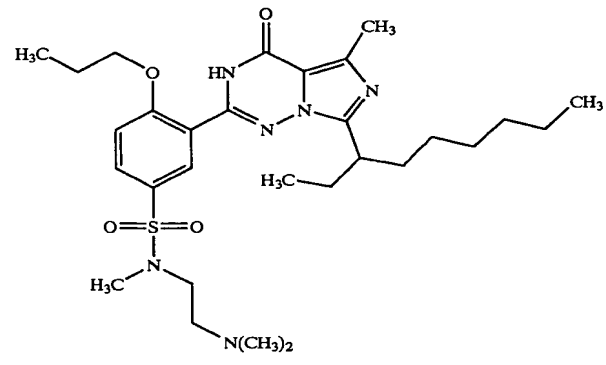
The preparation is carried out analogously to the procedure of Example 1 using 52 mg (0.102 mmol) of 4-propoxy-3-(5-methyl-4-oxo-7-(2-ethylheptyl)-3,4-dihydro[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 27 mg (0.255 mmol) of diethanolamine. This gives 41 mg (69.5%) of sulphonamide.

R_f=0.36 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 0.75–0.9 (m, 6H); 1.05 (t, 3H); 1.0–1.9 (m, 8H); 1.7–1.95 (m, 6H); 2.6 (s, 3H); 3.3 (t, 4H); 3.75 (t, 4H); 4.2 (t, 2H); 7.35 (d, 1H); 8.0 (dd, 1H); 8.1 (d, 1H).

EXAMPLE 70

2-[2-Propoxy-5-(N-methyl-N-(2-dimethylaminoethyl)-sulphonamido)-phenyl]-5-methyl-7-(2-ethylheptyl)-3H-imidazo[5,1-f][1,2,4] triazin-4-one



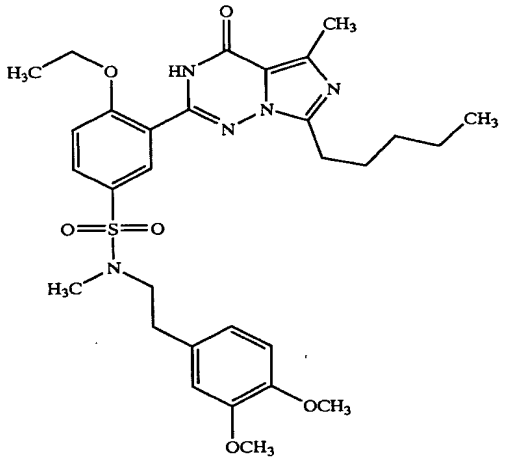
The preparation is carried out analogously to the procedure of Example 1 using 52 mg (0.102 mmol) of 4-propoxy-3-(5-methyl 4-oxo-7-(2-ethylheptyl)-3,4-dihydro[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 26 mg (0.255 mmol) of N-methyl-N-(2-dimethylaminoethyl) amine. This gives 42 mg (71.5%) of sulphonamide.

R_f=0.29 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 0.75–0.85 (m, 6H); 1.05 (t, 3H); 1.1–1.35 (m, 8H); 1.7–1.95 (m, 6H); 2.3 (s, 6H); 2.55 (t, 2H); 2.6 (s, 3H); 2.8 (s, 3H); 3.15 (t, 2H); 3.3 (m, 1H); 4.2 (t, 2H); 7.4 (d, 1H); 8.0 (dd, 1H); 8.05 (d, 1H).

EXAMPLE 71

2-[2-Ethoxy-5-(N-methyl-N-(2-(3,4-dimethoxyphenyl)-ethyl)-sulphonamido)-phenyl]-5-methyl-7-pentyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one



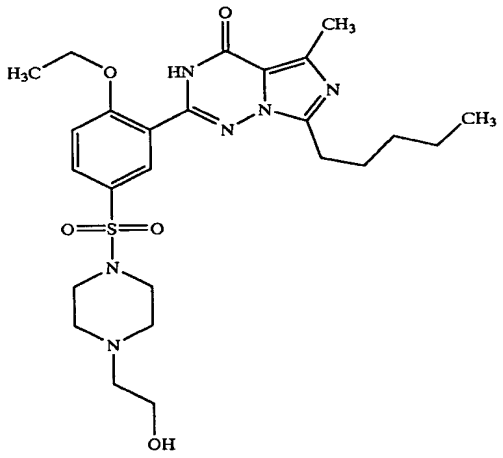
The preparation is carried out analogously to the procedure of Example 1 using 150 mg (0.342 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-pentyl-3,4-dihydro[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 167 mg (0.854 mmol) of N-methyl-N-(2-(3,4-dimethoxyphenyl)-ethylamine. This gives 195 mg (95.5%) of sulphonamide.

R_f=0.75 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 0.75 (t, 3H); 1.25–1.4 (m, 4H); 1.45 (t, 3H); 1.75 (quin., 2H); 2.55 (s, 3H); 2.75 (s, 3H); 2.8 (t, 2H); 2.95 (t, 2H); 3.75 (s, 6H); 4.25 (quar., 2H); 6.7 (dd, 1H); 6.8 (d, 1H); 6.85 (d, 1H); 7.3 (d, 1H); 7.9 (dd, 1H); 8.0 (d, 1H).

EXAMPLE 72

2-[2-Ethoxy-5-(4-(2-hydroxyethyl)-piperazine-1-sulphonyl)-phenyl]-5-methyl-7-pentyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one



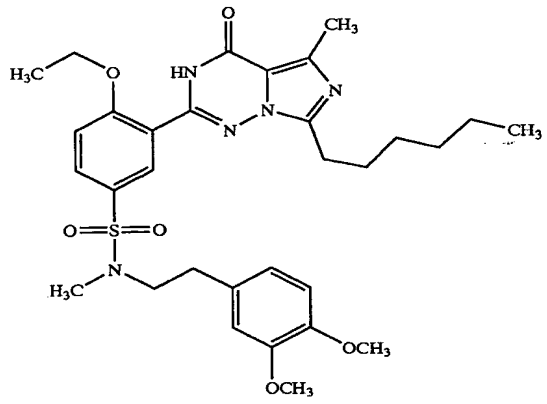
The preparation is carried out analogously to the procedure of Example 1 using 150 mg (0.342 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-pentyl-3,4-dihydro[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 111 mg (0.854 mmol) of 2-hydroxyethyl-piperazine. This gives 95 mg (52.4%) of sulphonamide.

R_f=0.55 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 0.9 (t, 3H); 1.3–1.4 (m, 4H); 1.45 (t, 3H); 2.95 (t, 2H); 3.05–3.1 (m, 4H); 3.6 (t, 2H); 4.3 (quar., 2H; 7.4 (d, 1H); 7.9 (dd, 1H); 8.0 (d, 1H).

EXAMPLE 73

2-[2-Ethoxy-5-(N-methyl-N-(2-(3,4-dimethoxyphenyl)-ethyl)-sulphonamido)-phenyl]-5-methyl-7-heptyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one



The preparation is carried out analogously to the procedure of Example 1 using 150 mg (0.321 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-heptyl-3,4-dihydro[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 140 mg (0.707

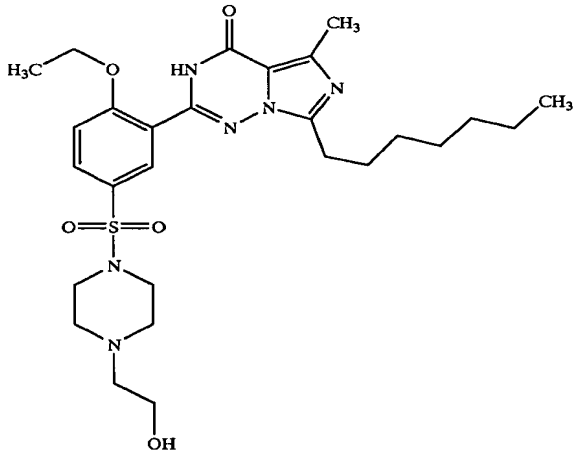
mmol) of N-methyl-N-(2-(3,4-dimethoxyphenyl)-ethylamine. This gives 112 mg (55.7%) of sulphonamide.

R_f=0.74 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 0.7–0.9 (t, 6H), 1.2–1.35 (m, 8H); 1.45 (t, 3H), 1.75 (quin., wH); 2.6 (s, 3H); 2.75 (s, 3H); 2.8 (t, 2H); 2.95 (t, 2H); 3.8 (s, 6H); 4.3 (quar., 2H); 6.7 (dd, 1H); 6.8–6.9 (m, 2H); 7.3 (d, 1H); 7.9 (dd, 1H); 8.0 (d, 1H).,

EXAMPLE 74

2-[2-Ethoxy-5-(4-(2-hydroxyethyl)-piperazine-1-sulphonyl)-phenyl]-5-methyl-7-heptyl-3H-imidazo [5,1-f][1,2,4]triazin-4-one



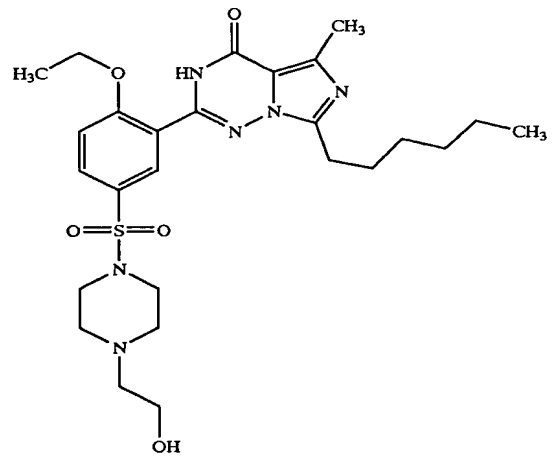
The preparation is carried out analogously to the procedure of Example 1 using 150 mg (0.321 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-heptyl-3,4-dihydro[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 92 mg (0.707 mmol) of 2-hydroxyethylpiperazine. This gives 160 mg (88.8%) of sulphonamide.

R_f=0.55 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 1.35 (t, 6H); 1.2–1.4 (m, 8H); 1.45 (t, 3H); 1.8 (quin., 2H); 2.5 (t, 2H); 3.0 (t, 2H); 3.05–3.1 (m, 4H); 3.3 (t, 2H); 3.6 (t, 2H); 4.3 (quar., 2H); 7.4 (d, 1H); 7.9 (dd, 1H); 8.0 (d, 1H).

EXAMPLE 75

2-[2-Ethoxy-5-(4-(2-hydroxyethylpiperazine-1-sulphonyl)-phenyl]-5-methyl-7-hexyl-3H-imidazo[5, 1-f][1,2,4]-triazin-4-one



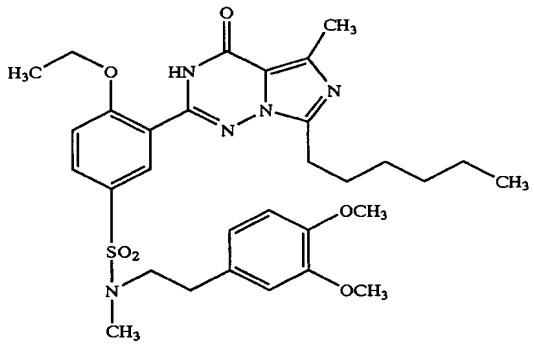
The preparation is carried out analogously to the procedure of Example 1 using 150 mg (0.33 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-n-hexyl-3,4-dihydro-imidazo[5,1-f][1, 2,4]-triazin-2-yl)-benzenesulphonyl chloride and 90 mg (0.725 mmol) of 2-hydroxyethylpiperazine. This gives 90 mg (49.8%) of sulphonamide.

R_f=0.57 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 0.75 (t, 3H);1.15–1.3 (m, 6H);1.35 (t, 3H); 1.7 (quin., 2H); 2.4 (t, 2H); 2.5 (s, 3H) 2.5–2.55 (m, 4H); 2.9 (t, 2H); 2.95–3.0 (m, 4H); 3.5 (t, 2H); ,2 (quar., 2H); 7.3 (d, 1H); 7.85 (dd, 1H), 7.9 (d, 1H).

EXAMPLE 76

2-[2-Ethoxy-5-(N-methyl-N-(2-(3,4-dimethoxyphenyl)-ethyl)sulphonamido)-phenyl]-5-methyl-7-hexyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



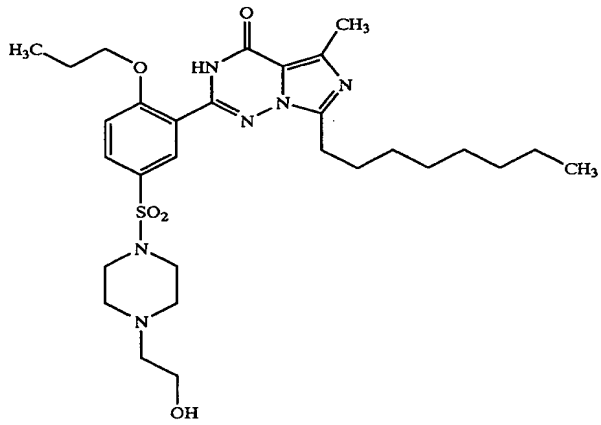
The preparation is carried out analogously to the procedure of Example 1 using 150 mg (0.33 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-n-hexyl-3,4-dihydro-imidazo[5,1-f][1, 2,4]-triazin-2-yl)-benzenesulphonyl chloride and 140 mg (0.725 mmol) of N-methyl-N-(2-(3,4-dimethoxyphenyl)-ethylamine. This gives 24.7%) of sulphonamide.

R_f=0.72 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 0.75 (t, 3H); 1.1–1.25 (m, 6H); 1.35 (t, 3H); 1.65 (quin., 2H); 2.5 (s, 3H); 2.65 (s, 3H); 2.7 (t, 2H); 2.85 (t, 2H); 3.65 (s, 6H); 4.15 (quar., 2H); 6.6–6.75 (m, 3H); 7.2 (d, 1H); 7.75 (dd, 1H); 7.9 (d, 1H).

EXAMPLE 77

2-[2-Ethoxy-5-(4-(2-hydroxyethylpiperazine-1-sulphonyl)-phenyl]-5-methyl-7-nonyl-3H-imidazo[5, 1-f][1,2,4]-triazin-4-one



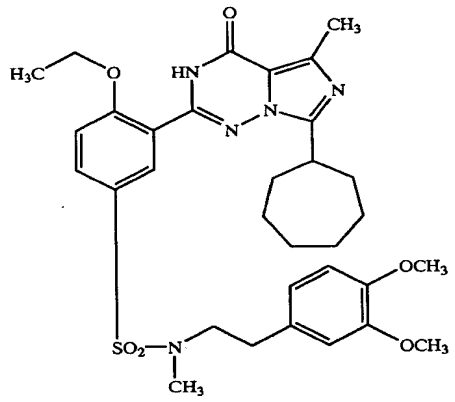
The preparation is carried out analogously to the procedure of Example 1 using 200 mg (0.4 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-n-nonyl-3,4-dihydro-imidazo[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride and 120 mg (0.89 mmol) of 2-hydroxyethyl-piperazine. This gives 85 mg (35.7%) of sulphonamide.

R_f=0.45 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 0.75 (t, 3H); 1.1–1.3 (m, 12H); 1.4 (t, 3H); 1.7 (quin., 2H); 2.4 (t, 2H);2.5 (s, 3H); 2.5–2.6 (m, 4H); 2.9 (t, 2H); 2.95–3.05 (m, 4H); 3.5 (t, 2H); 4.3 (quar., 2H); 7.3 (d, 1H); 7.8 (dd, 1H); 7.9 (d, 1H).

EXAMPLE 78

2-[2-Ethoxy-5-(N-methyl-N-(2-(3,4-dimethoxyphenyl-ethyl)-sulphonamido)-phenyl]-5-methyl-7-nonyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



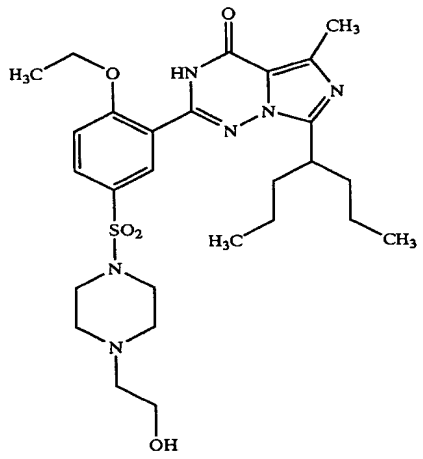
The preparation is carried out analogously to the procedure of Example 1 using 200 mg (0.4 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-n-nonyl-3,4-dihydro-imidazo[5,1-f][1,2,4]triazin-2-yl)-benzenesulphonyl chloride and 170 mg (0.89 mmol) of N-methyl-N-(2-(3,4-dimethoxy)phenyl)-ethylamine. This gives 142 mg (52.8%) of sulphonamide.

R_f=0.74 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 0.7 (t, 3H); 1.1–1.3 (m, 12H); 1.4 (t, 3H); 1.7 (quin., 2H); 2.5 (s, 3H); 2.7 (s, 3H); 2.75 (t, 2H); 2.9 (t, 2H); 3.3 (t, 2H); 3.7 (s, 6H); 4.7 (quar., 2H); 6.6–6.8 (m, 3H); 7.2 (d, 1H), 7.7 (dd, 1H); 7.95 (d, 1H).

EXAMPLE 79

2-[2-Ethoxy-5-(4-(2-hdyroxyethylpiperazine-1-sulphonyl)phenyl]-5-methyl-7-(2-n-propylbutyl)-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



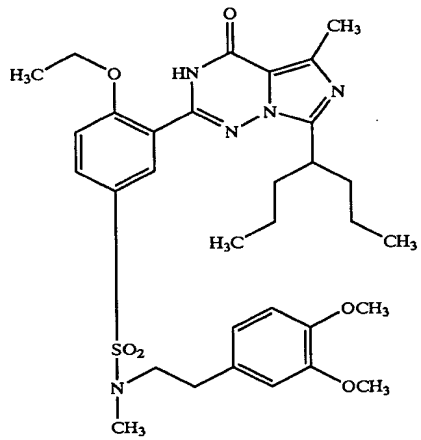
The preparation is carried out analogously to the procedure of Example 1 using 150 mg (0.32 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-(2-n-propylbutyl)-3,4-dihydro-imidazo[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 50 mg (0.385 mmol) of 2-hydroxyethyl-piperazine. This gives 150 mg (83.3%) of sulphonamide.

R_f=0.62 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 0.75 (t, 6H); 1.1–1.25 (m, 4H); 1.4 (t, 3H); 1.6–1.7 (m, 2H); 1.75–1.85 (m, 2H); 2.45 (t, 2H); 2.5 (s, 3H); 2.5–2.55 (m, 4H); 3.0 (m, 4H); 3.4 (hept., 1H); 2.55 (t, 2H); 4.25 (quar., 2H); 7.35 (d, 1H); 7.85 (dd, 1H); 7.95 (d, 1H).

EXAMPLE 80

2-[2-Ethoxy-5-(N-methyl-N-(2-(3,4-dimethoxyphenyl)-ethyl)-sulphonamido)-phenyl]-5-methyl-7-(2-n-propylbutyl)-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



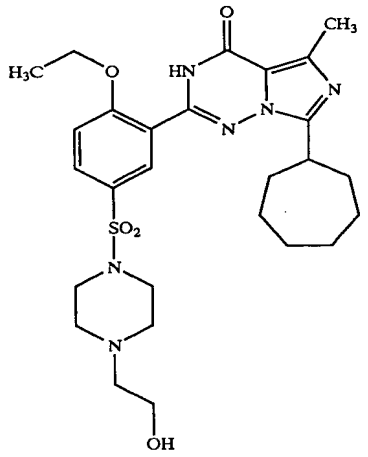
The preparation is carried out analogously to the procedure of Example 1 using 150 mg (0.32 mmol) of 4-ethoxy-

3-(5-methyl-4-oxo-7-(2-n-propylbutyl)-3,4-dihydro-imidazo[5,1-f][1,2,4]-triazin-2-yl)-benzenesulphonyl chloride and 80 mg (0.385 mmol) of N-methyl-N-(2-(3,4-dimethoxyphenyl)-ethylamine. This gives 166 mg (82.6%) of sulphonamide.

M.p.: 131° C. (ethyl acetate/diethyl ether).

EXAMPLE 81

2-[2-Ethoxy-5-(4-(2-hydroxyethylpiperazine-1-sulphonyl)-phenyl]-5-methyl-7-cycloheptyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one

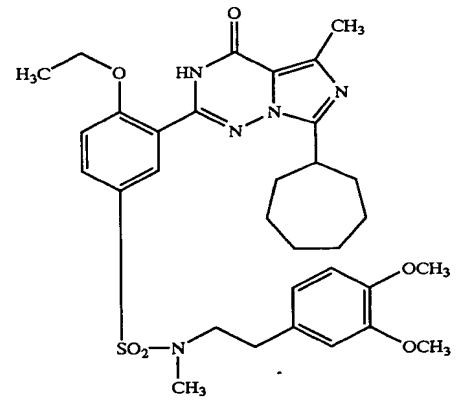


The preparation is carried out analogously to the procedure of Example 1 using 200 mg (0.43 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cycloheptyl-3,4-dihydro-imidazo[5,1-f]-[1,2,4]-triazin-2-yl-benzenesulphonyl chloride and 120 mg (0.946 mmol) of 2-hydroxyethyl-piperazine. This gives 158 mg (65.7%) of sulphonamide.

R_f=0.55 (CH_2Cl_2/MeOH 10:1)

EXAMPLE 82

2-[2-Ethoxy-5-(N-methyl-N-(2-(3,4-dimethoxyphenyl)-ethyl)-sulphonamido)-phenyl]-5-methyl-7-cycloheptyl-3H-imidazo[5,1-f][1,2,4]-triazin-4-one



The preparation is carried out analogously to the procedure of Example 1 using 300 mg (0.645 mmol) of 4-ethoxy-3-(5-methyl-4-oxo-7-cycloheptyl-3,4-dihydro-imidazo[5,1-f]-[1,2,4]-triazin-2-yl-benzenesulphonyl chloride and 280 mg (1.42 mmol) of N-methyl-N-(2-(3,4-dimethoxyphenyl)-ethylamine. This gives 256 mg (63.6%) of sulphonamide.

R_f=0.66 (CH_2Cl_2/MeOH 10:1)

^{1}H-NMR (CD_3OD): 1.45 (t, 2H); 1.5–1.7 (m, 9H); 1.7–2.0 (m,6H); 2.55 (s, 3H); 2.75 (s, 3H); 2.8 (t, 2H); 3.35 (t, 2H); 3.45 (quin., 1H); 3.7 (s, 6H); 4.25 (quar., 2H): 6.65–6.8 (m, 3H); 7.25 (d, 1H); 7.85 (dd, 1H); 8.0 (d, 1H).

The sulphonamides listed in the tables below were prepared by automatic parallel synthesis from the corresponding sulphonyl chlorides and the corresponding amines using one of the three standard procedures below.

The purity of the final product was determined by means of HPLC, and they were characterized by LC-MS. The number given in the column % (HPLC) is the content of the end product characterized by the molecular peak. Standard procedure A was used with amines having acidic functionalities, standard procedure B was used with amines having neutral functionalities, standard procedure C was used with amines having additional basic functionalities.

Compounds listed in the tables below and having optically a free nitrogen valency are, in principle, to be understood as —NH— radical.

Standard Procedure A

Reaction of Amines Having Acidic Functionalities

0.05 mmol of amine, 0.042 mmol of sulphonyl chloride and 0.10 mmol of Na_2CO_3 are initially charged, and 0.5 ml of a mixture of THF/H_2O is pipetted in by hand. After 24 h at room temperature, the mixture is admixed with 0.5 ml of 1 M H_2SO_4 solution and filtered through a two-phase cartridge (500 mg of Extrelut (upper phase)) and 500 mg of SiO_2, mobile phase ethyl acetate). The product is obtained after concentrating the filtrate under reduced pressure.

Standard Procedure B

Reaction of Amines Having Neutral Functionalities

0.125 mmol of amine are initially charged and 0.03 mmol of sulphonyl chloride as a solution in 1,2-dichloroethane is pipetted in by the synthesizer. After 24 h, the mixture is admixed with 0.5 ml of 1 M H_2SO_4 and filtered through a two-phase cartridge (500 mg of Extrelut (upper phase) and 500 mg of SiO_2, mobile phase: ethyl acetate). The filtrate is concentrated under reduced pressure.

Standard Procedure C

Reaction of Amines Having Basic Functionalities

0.05 mmol of amine are initially charged and 0.038 mmol of sulphonyl chloride as a solution in 1,2-dichloroethane and 0.05 mmol of triethylamine as a solution in 1,2-dichloroethane are pipetted in by the synthesizer. After 24 h. the solution is initially admixed with 3 ml of saturated $NaHCO_3$ solution and the reaction mixture is filtered through a two-phase cartridge. The product is obtained after concentrating the filtrate under reduced pressure.

All reactions are monitored by thin-layer chromatography. If the reaction is not complete after 24 h at room temperature, the mixture is heated at 60° C. for a further 12 h and the experiment is subsequently terminated.

TABLE 1

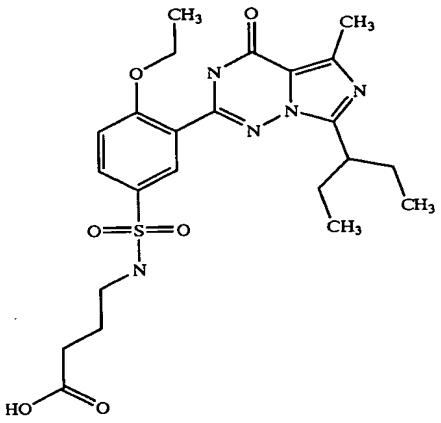
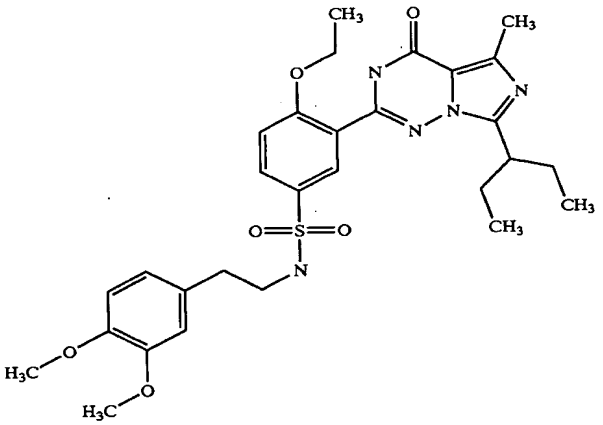
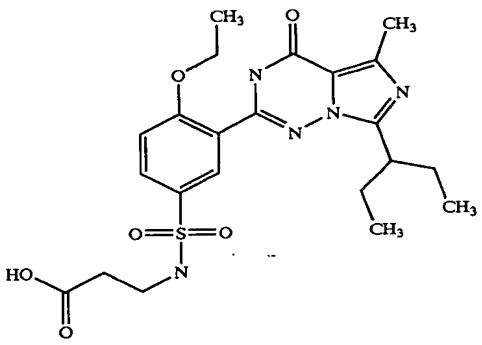
Ex. No.	Structure	MW	% (HPLC)*
83		505.6	76
84		583.71	89
85		491.57	56

TABLE 1-continued

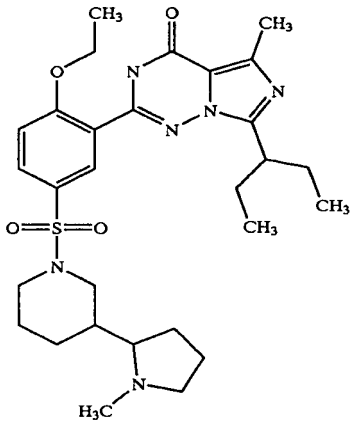
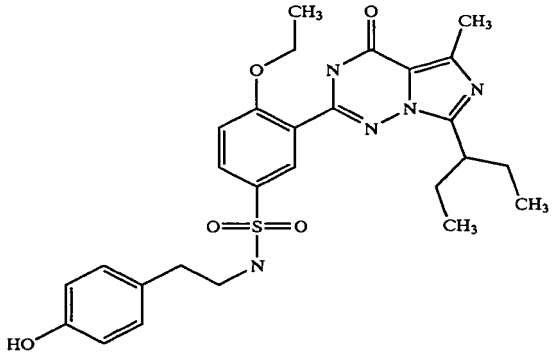
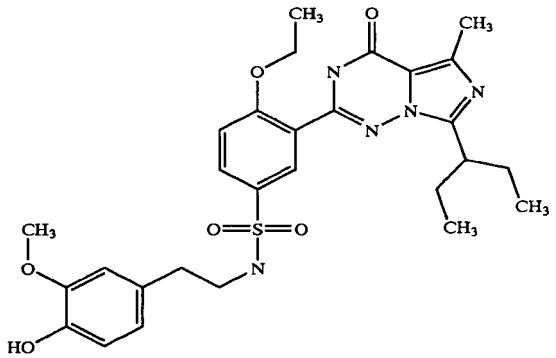
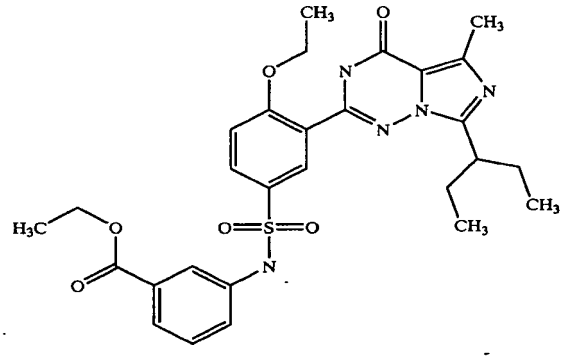
86		570.76	60
87		539.66	87
88		569.69	88
89		567.67	82

TABLE 1-continued

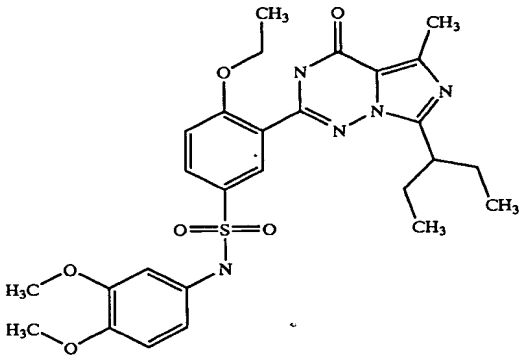
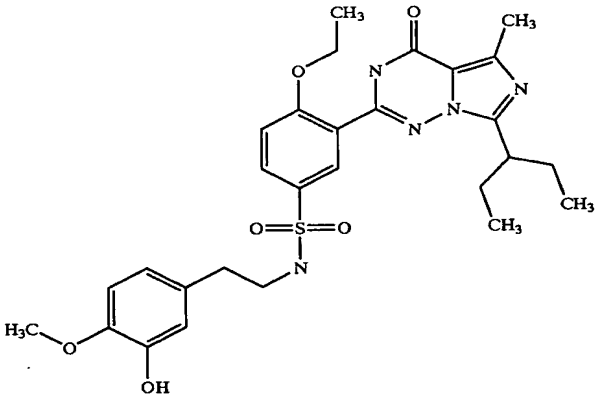
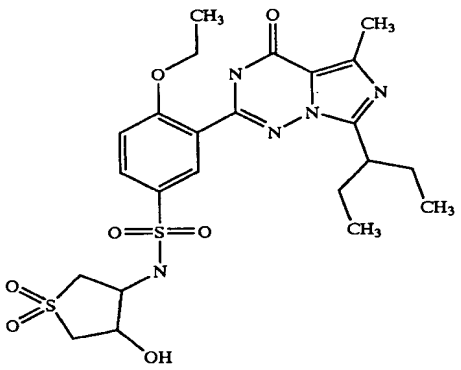
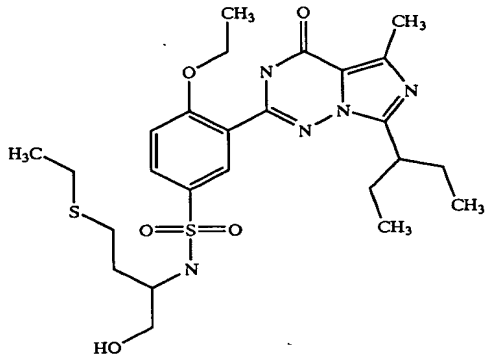
90		555.66	91
91		569.69	77
92		553.66	54
93		551.73	62

TABLE 1-continued

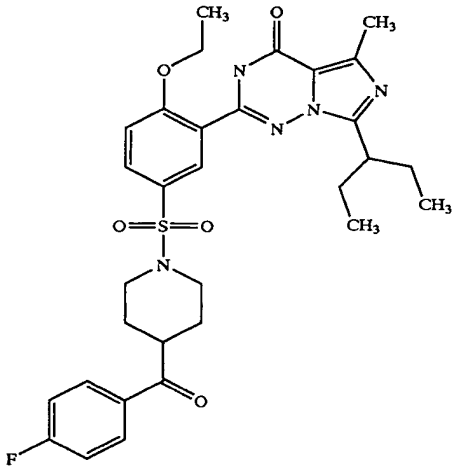
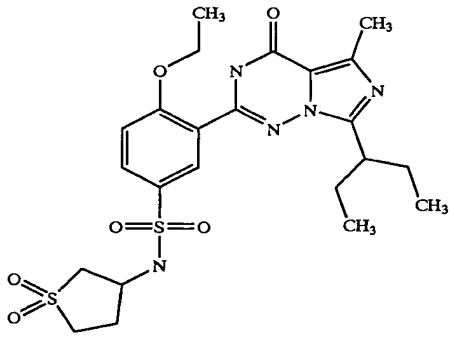
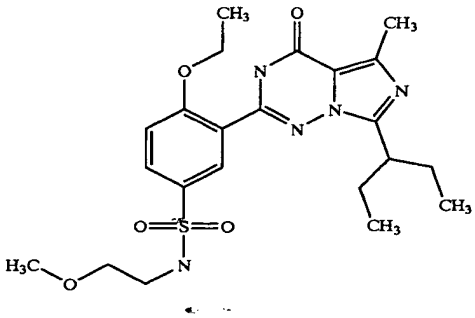
94		609.73	60
95		537.66	88
96		477.59	97

TABLE 1-continued

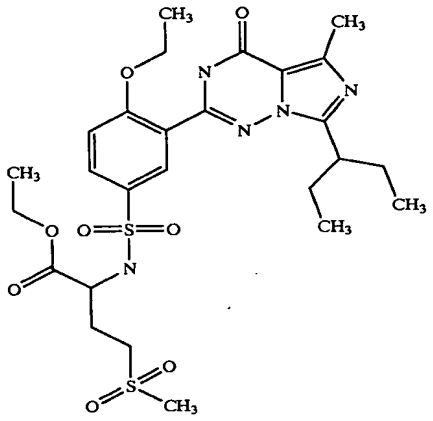
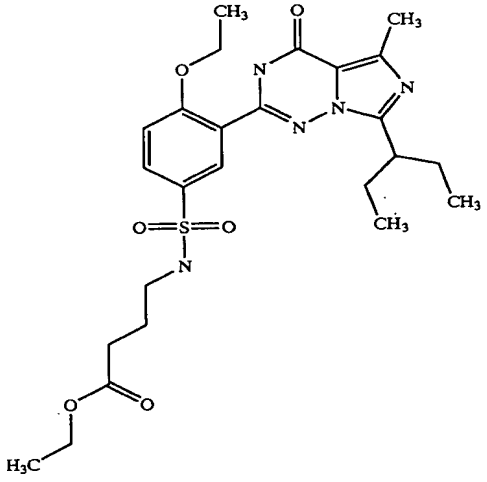
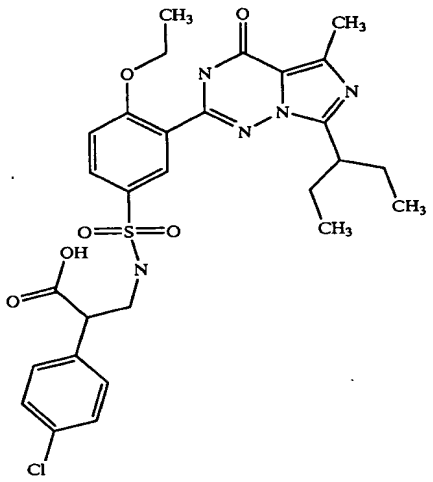
97		611.74	52
98		533.65	85
99		602.11	NMR

TABLE 1-continued

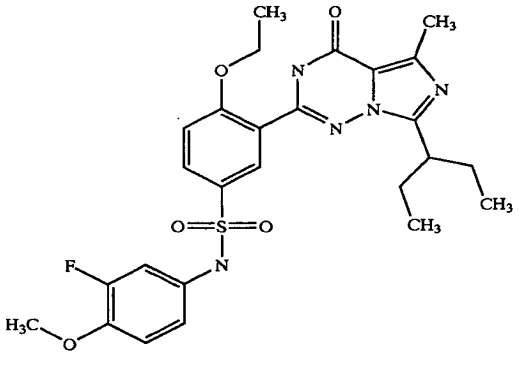
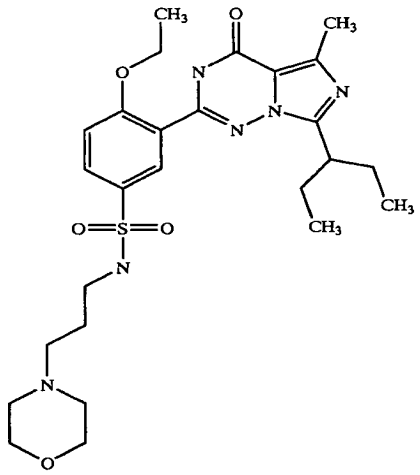
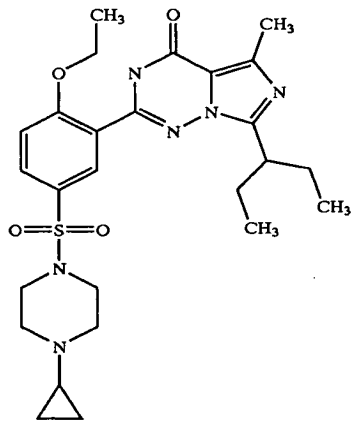
100		543.62	88
101		546.69	82
102		528.68	82

TABLE 1-continued

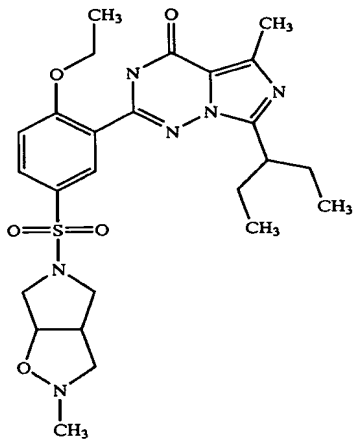
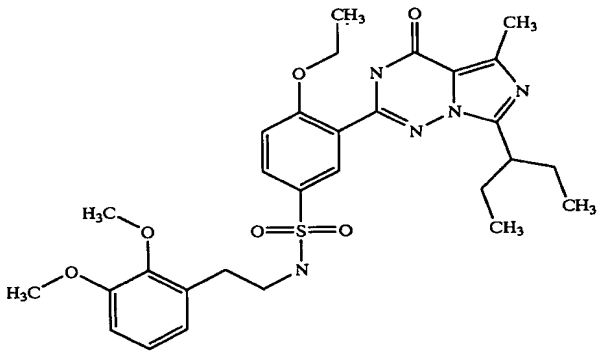
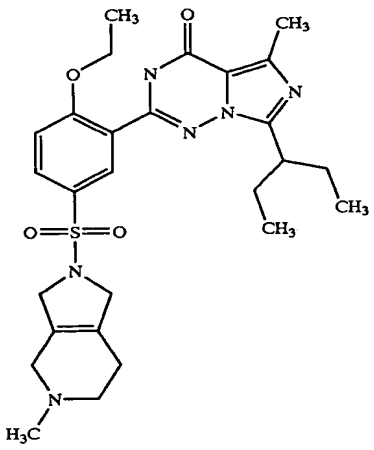
103		530.65	77
104		583.71	91
105		540.69	58

TABLE 1-continued

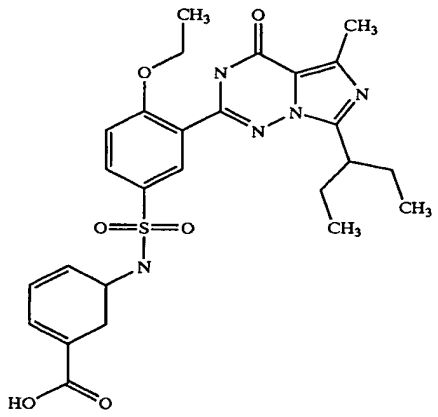
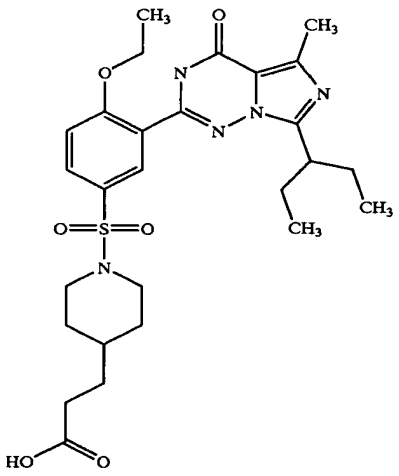
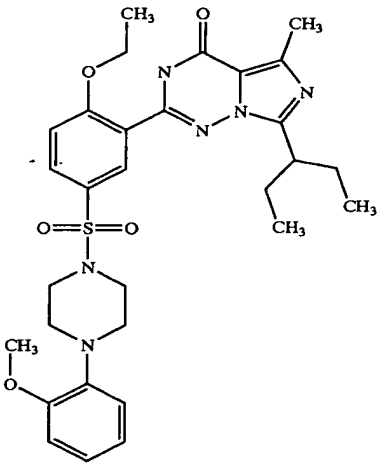
106		541.63	38
107		559.69	60
108		594.74	88

TABLE 1-continued

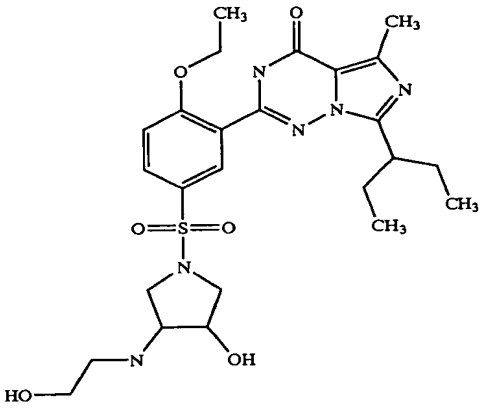
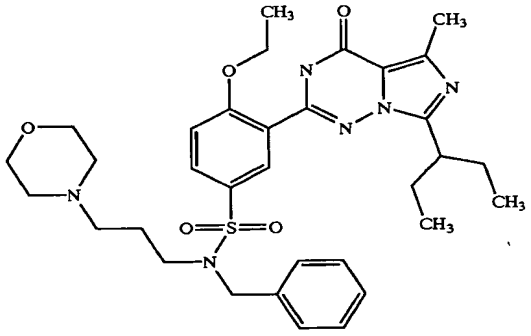
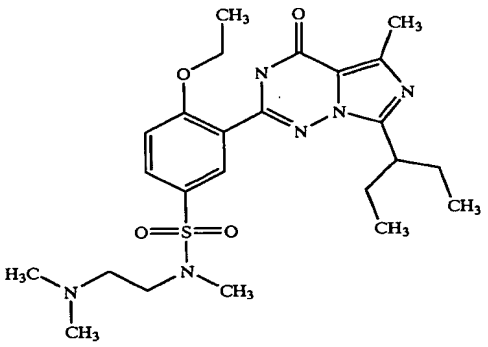
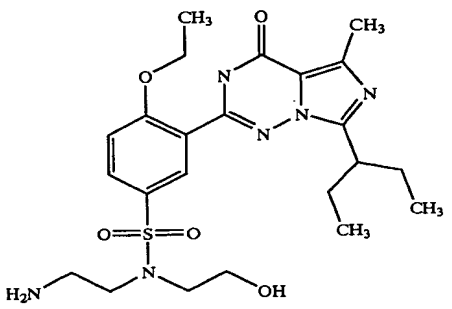
109		548.67	61
110		636.82	85
111		504.66	67
112		506.63	57

TABLE 1-continued

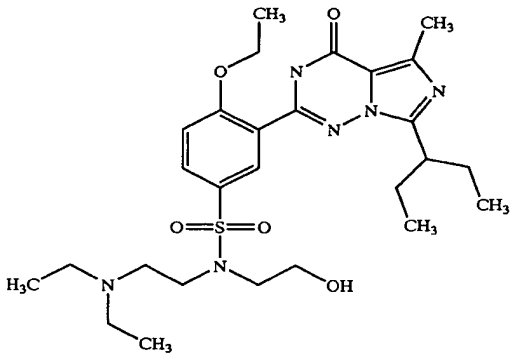
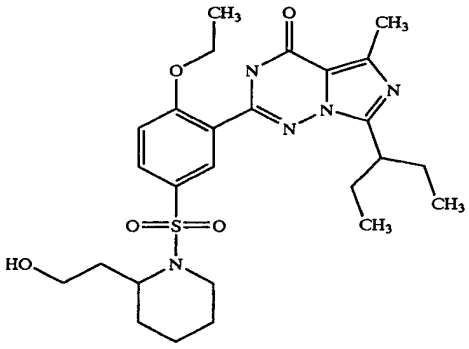
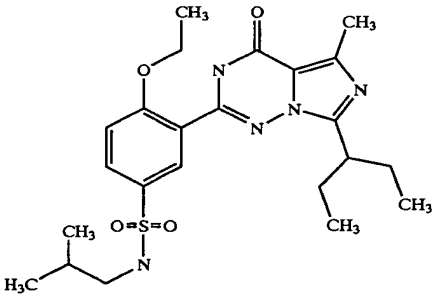
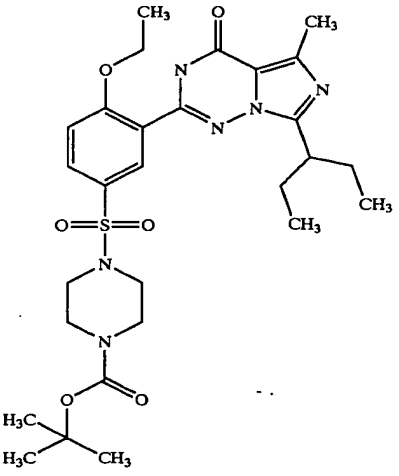
113		562.74	84
114		531.68	61
115		475.61	90
116		588.73	82

TABLE 1-continued

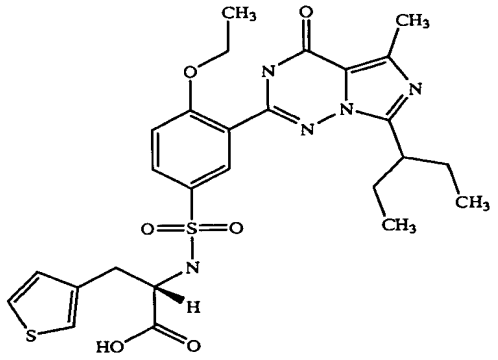
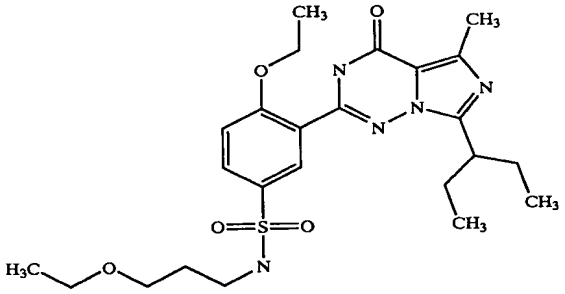
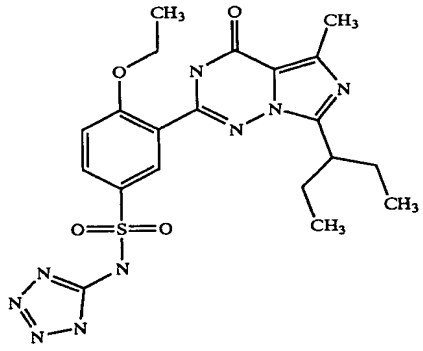
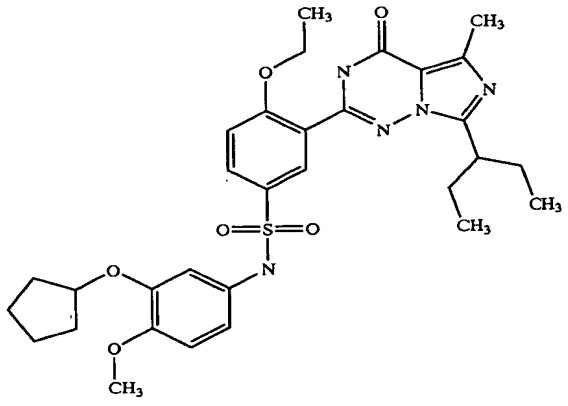
117		573.69	52
118		505.64	92
119		487.54	>58
120		609.75	86

TABLE 1-continued

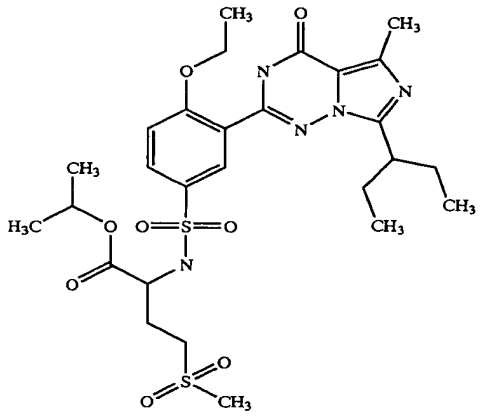
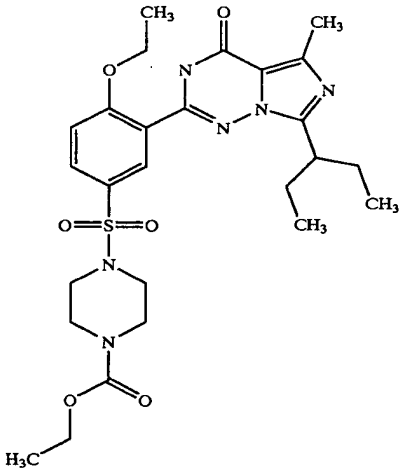
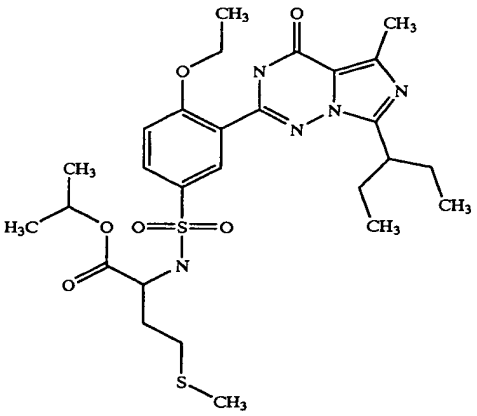
121		625.77	98
122		560.68	90
123		593.77	46

TABLE 1-continued

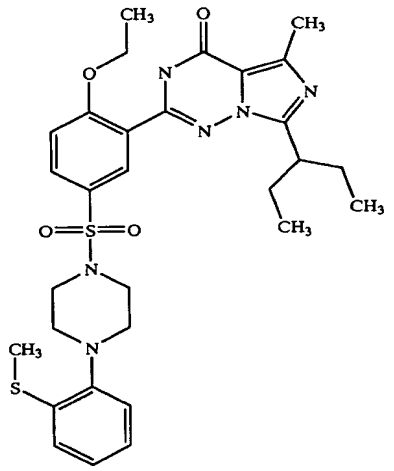
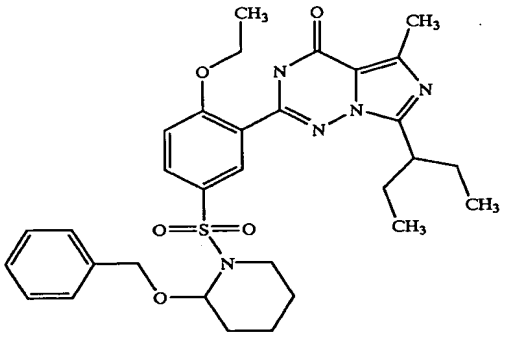
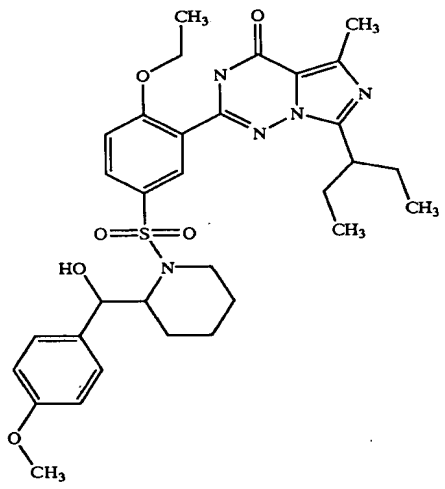
124		610.8	64
125		593.75	84
126		623.78	85

TABLE 1-continued

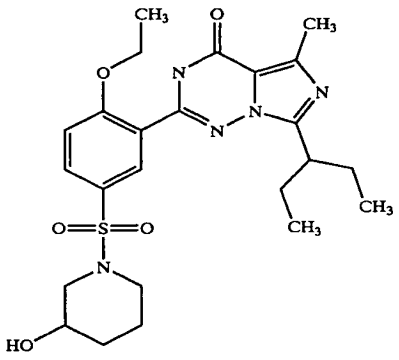
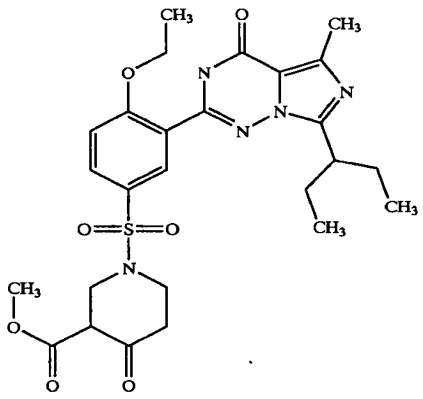
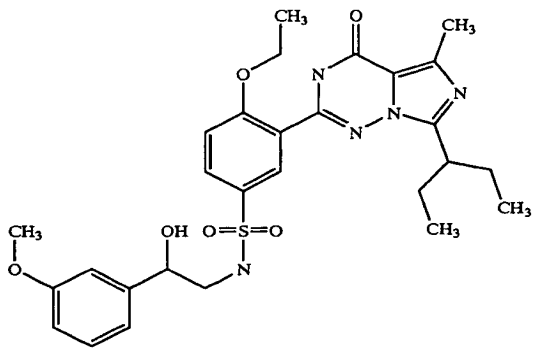
127		503.63	89
128		559.65	58
129		569.69	70

TABLE 1-continued

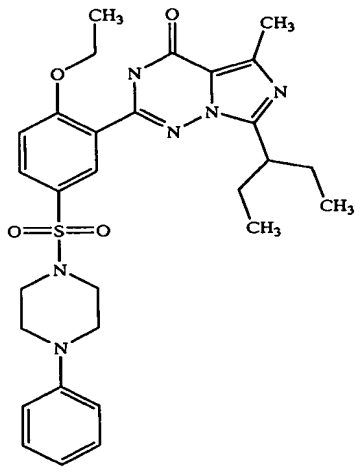
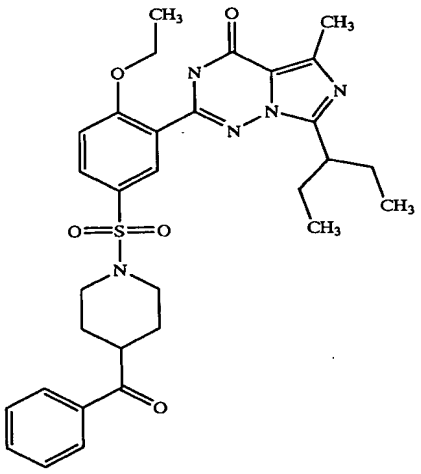
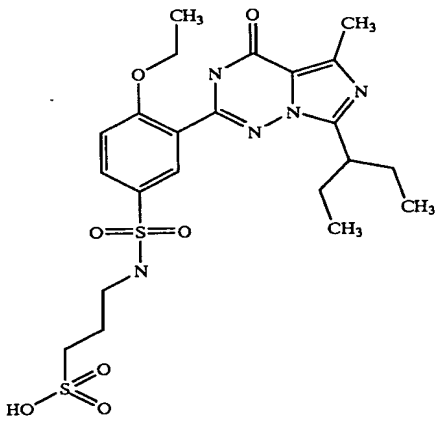
130		564.71	76
131		591.74	77
132		541.65	66

TABLE 1-continued

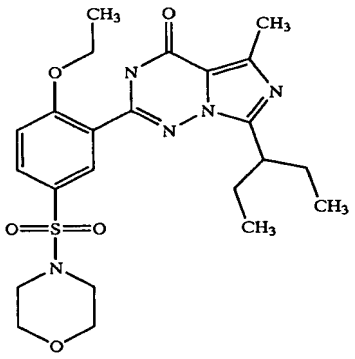
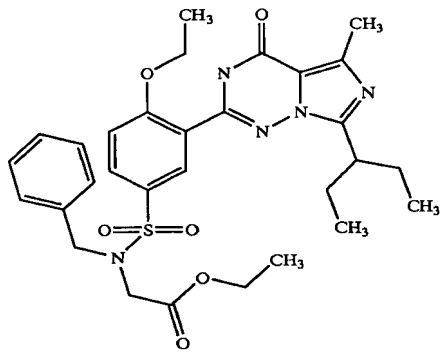
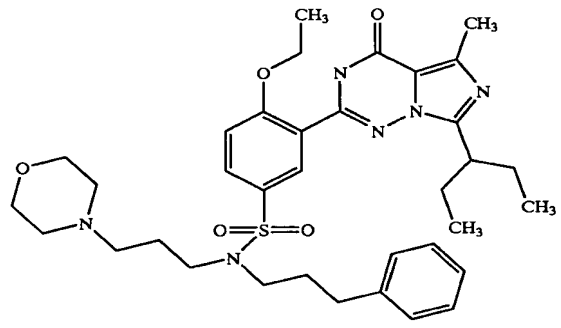
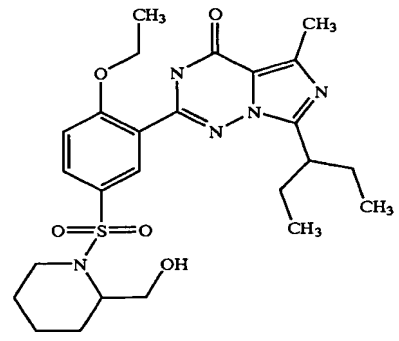
133		489.6	83
134		595.72	84
135		664.87	70
136		517.65	77

TABLE 1-continued

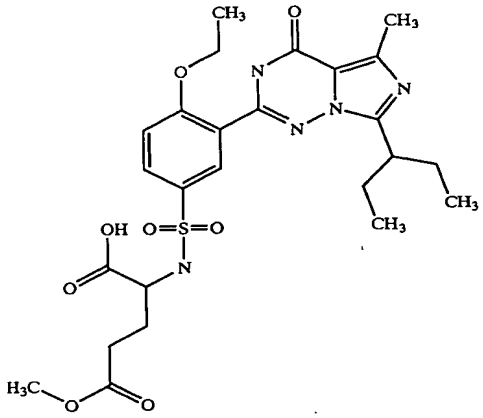
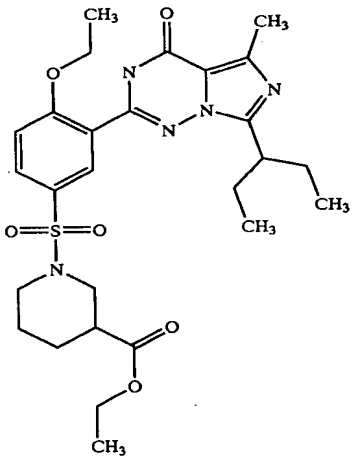
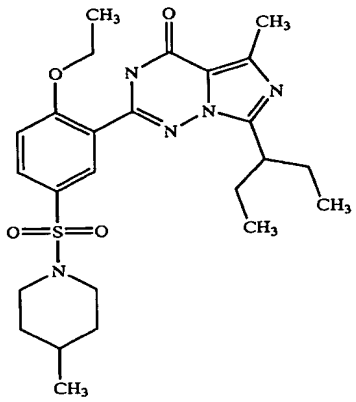
137		563.63	31
138		559.69	88
139		501.65	81

TABLE 1-continued

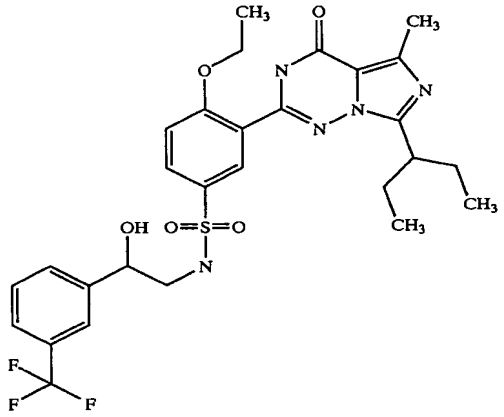
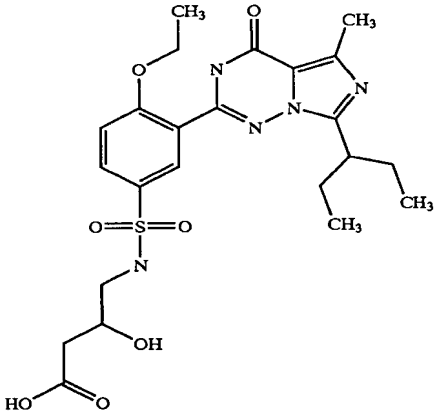
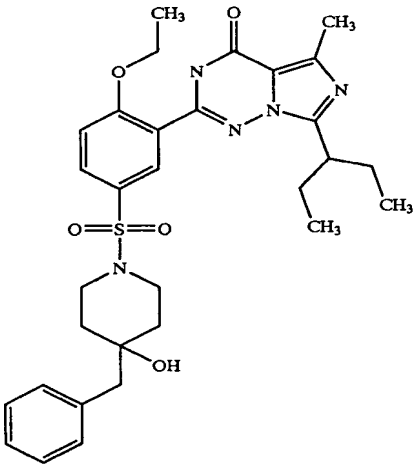
140		607.66	86
141		521.6	37
142		593.75	82

TABLE 1-continued

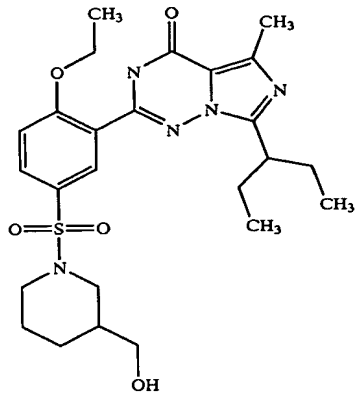
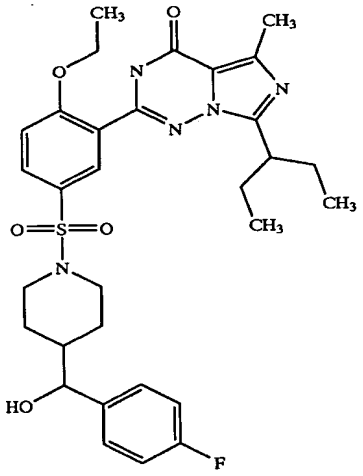
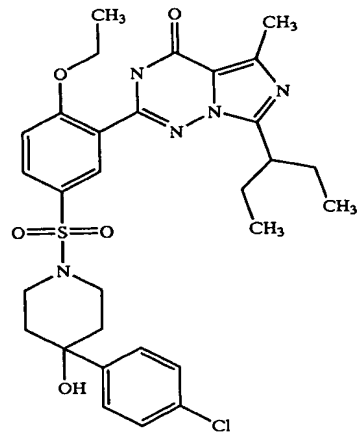
143		517.65	85
144		611.74	67
145		614.17	78

TABLE 1-continued

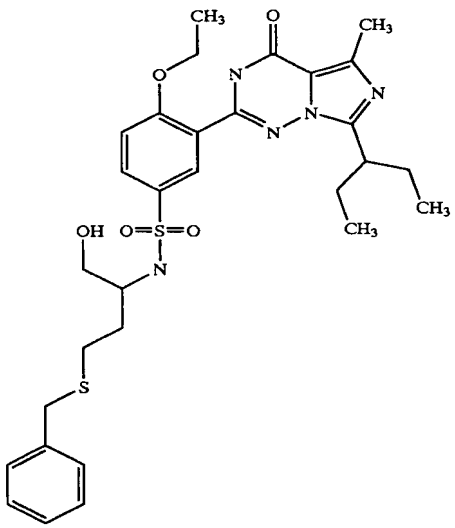
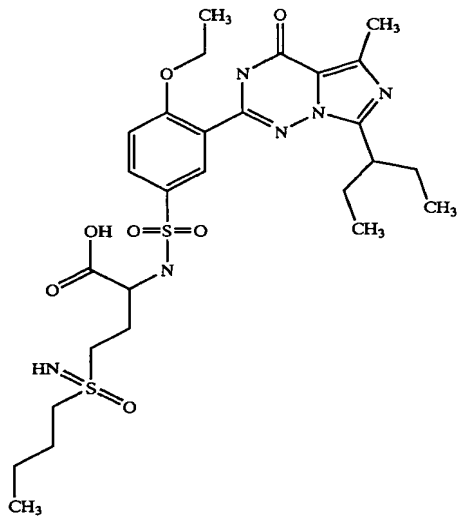
146		613.8	47
147		624.78	52

TABLE 1-continued

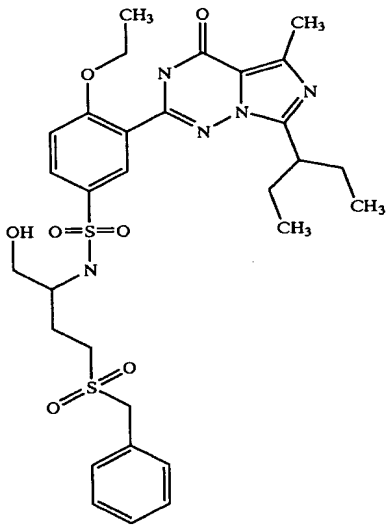
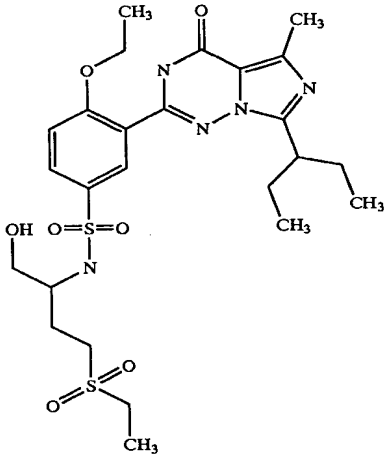
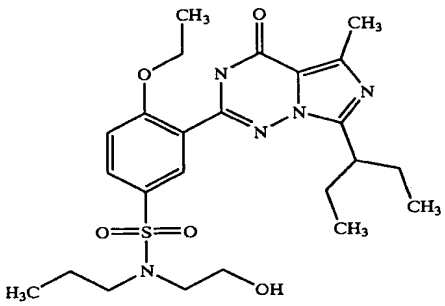
148		645.8	69
149		583.73	75
150		505.64	78

TABLE 1-continued

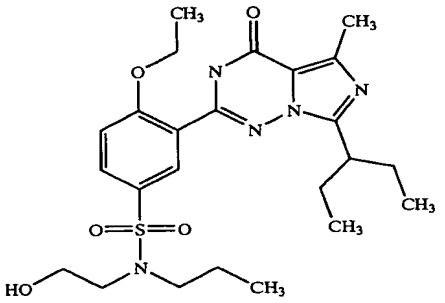
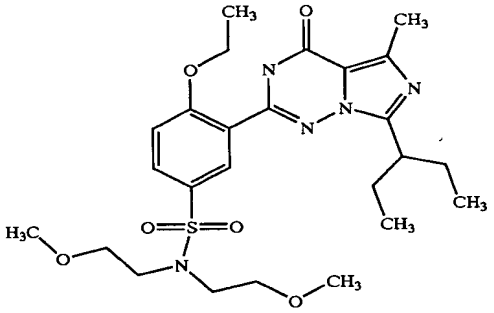
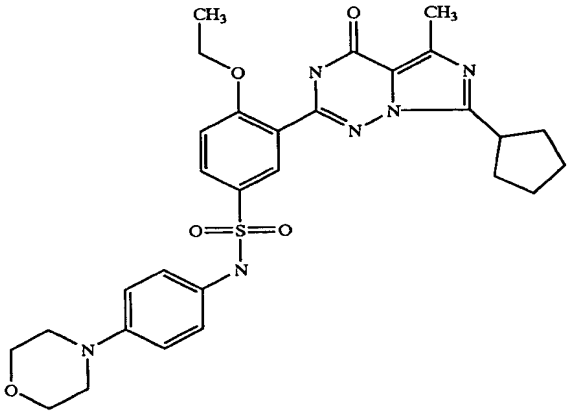
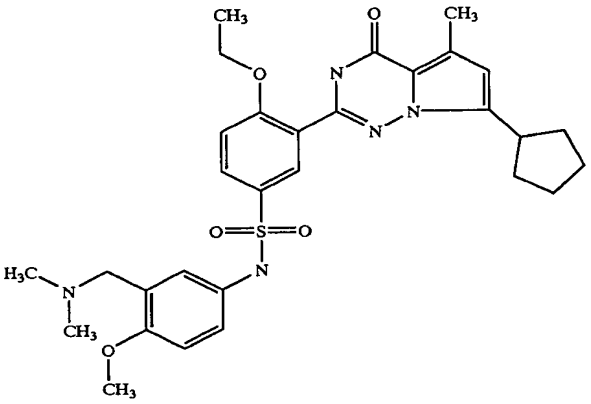
151		491.61	83
152		535.67	81
153		578.7	70
154		580.7	75

TABLE 1-continued

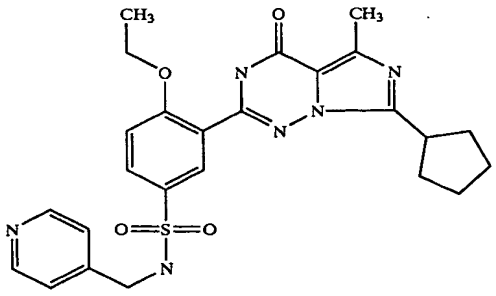
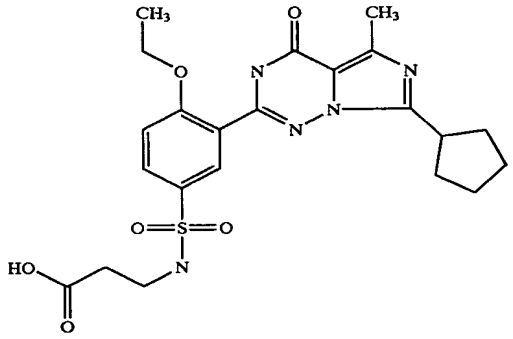
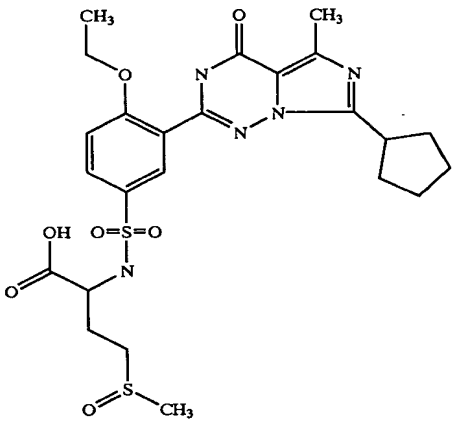
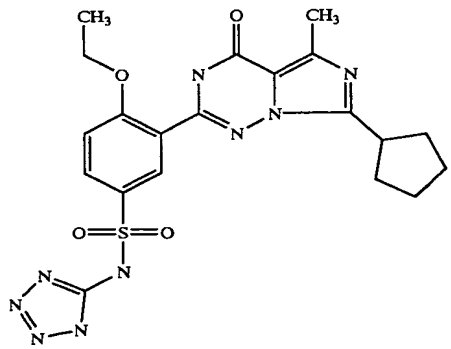
155		508.6	62
156		489.6	72
157		565.7	76
158		485.5	42

TABLE 1-continued

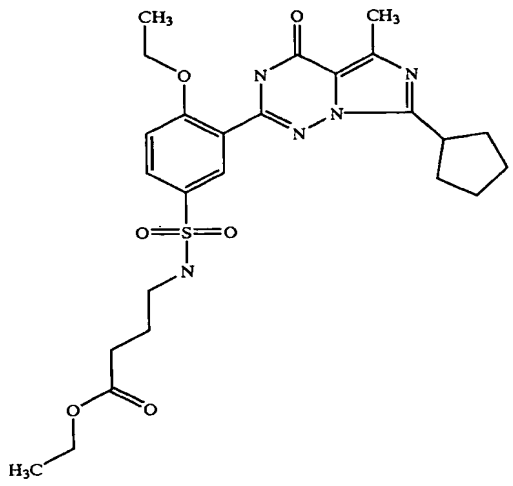
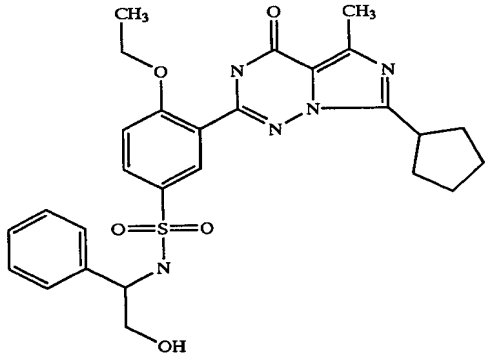
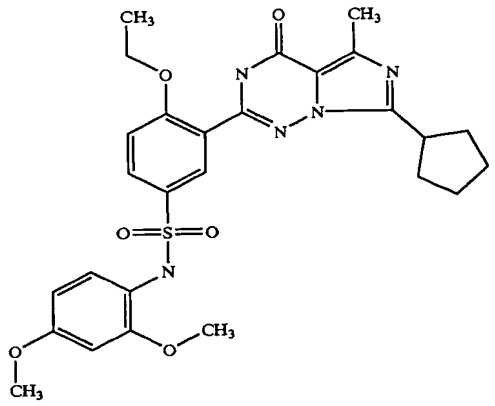
159		531.6	88
160		537.6	80
161		553.6	78

TABLE 1-continued

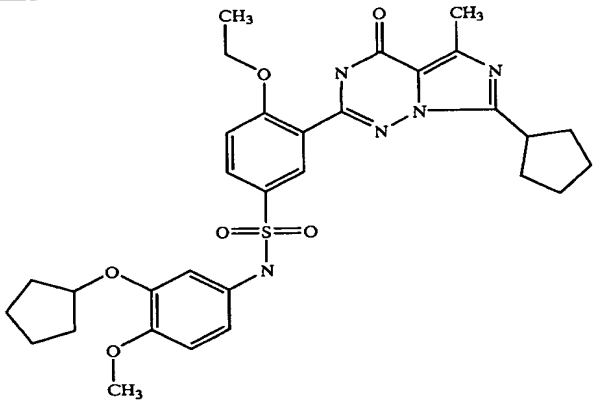
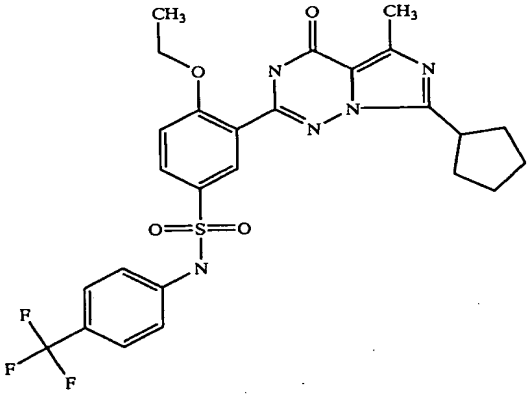
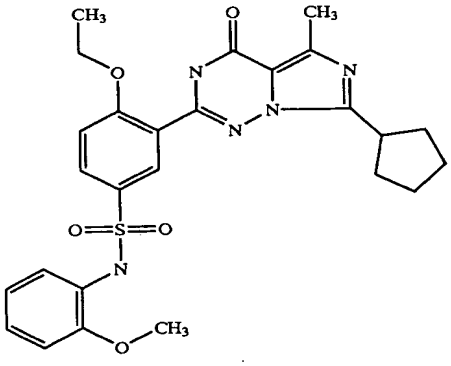
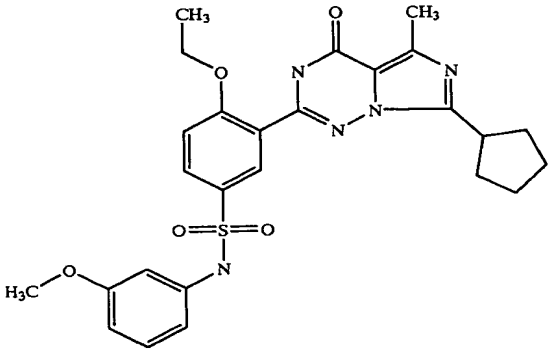
162		607.7	75
163		561.6	80
164		523.6	83
165		523.6	84

TABLE 1-continued

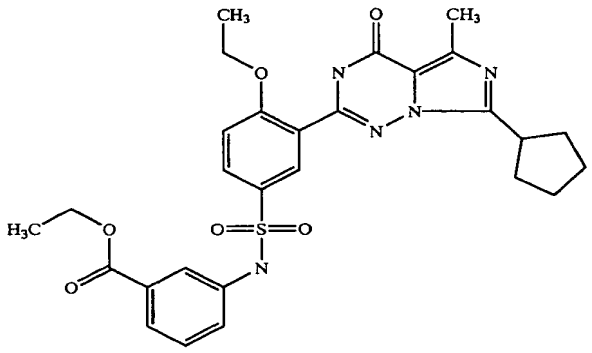
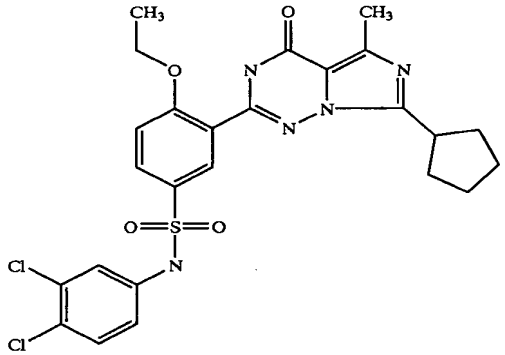
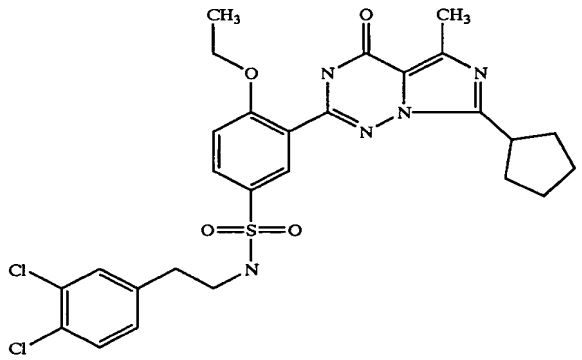
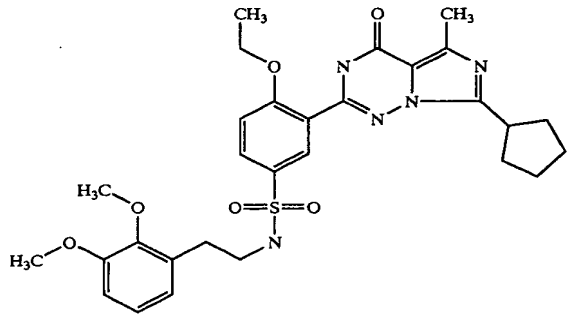
166		565.7	81
167		562.5	63
168		590.5	82
169		581.7	81

TABLE 1-continued

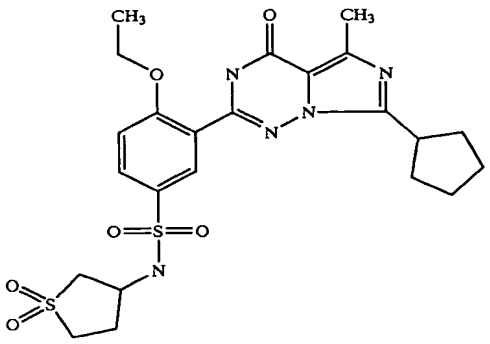
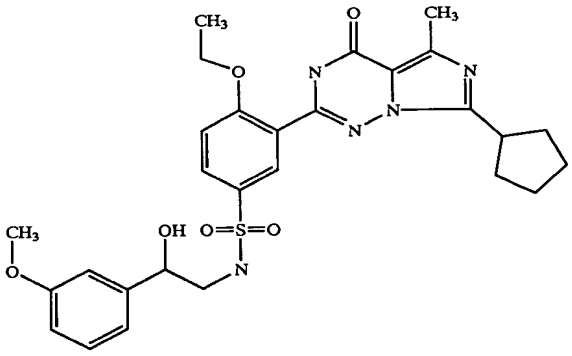
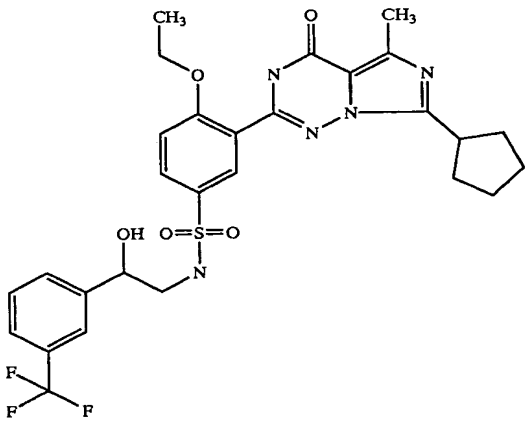
170		535.6	79
171		567.7	55
172		605.6	81

TABLE 1-continued

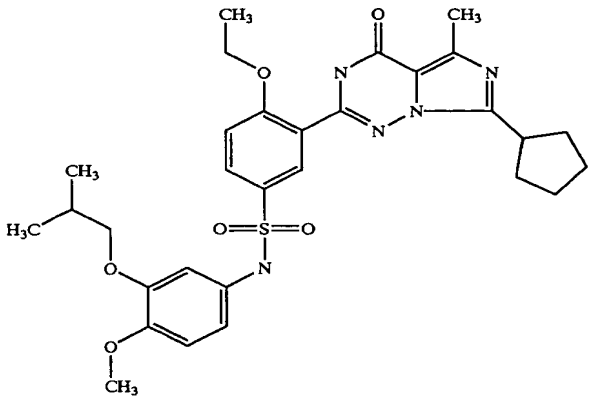
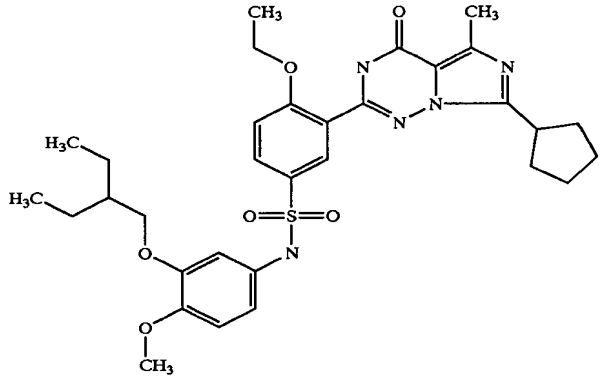
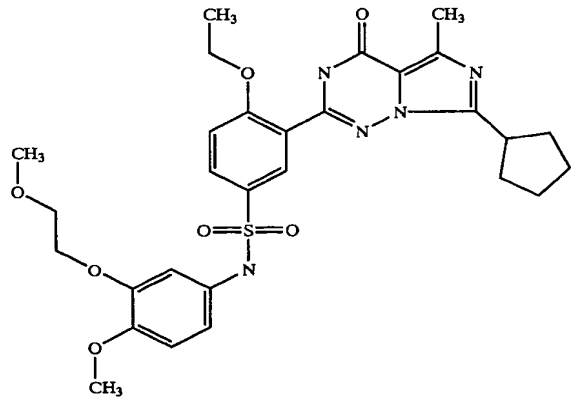
173		595.7	79
174		623.8	79
175		597.7	59

TABLE 1-continued

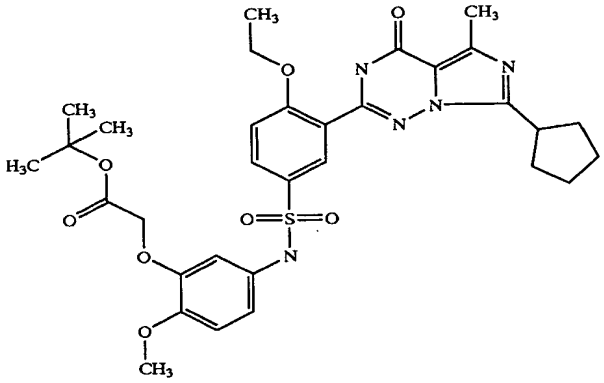
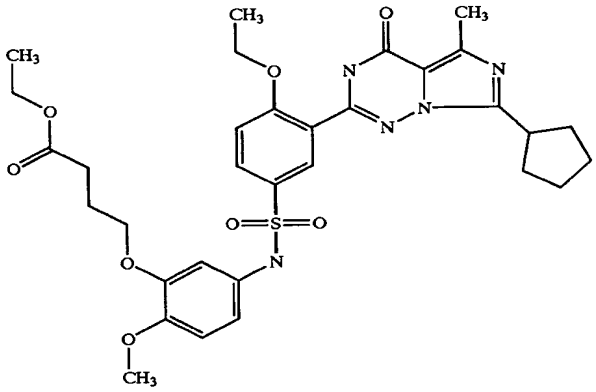
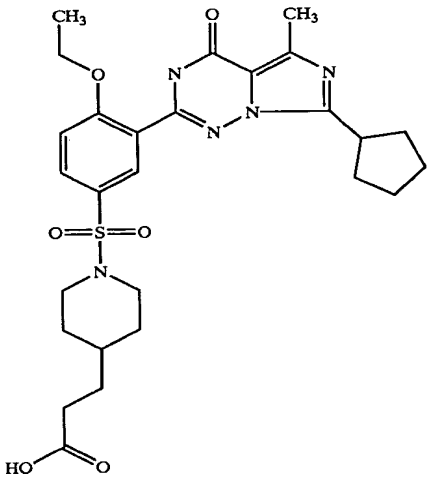
176		653.8	41
177		653.8	82
178		557.7	83

TABLE 1-continued

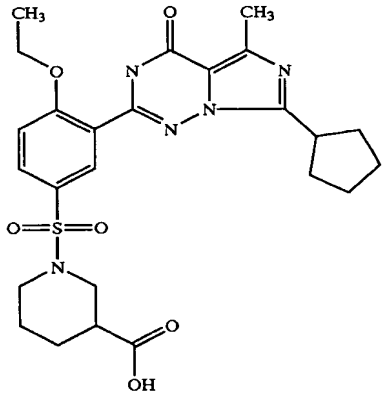
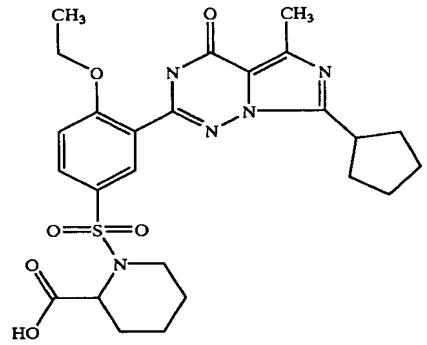
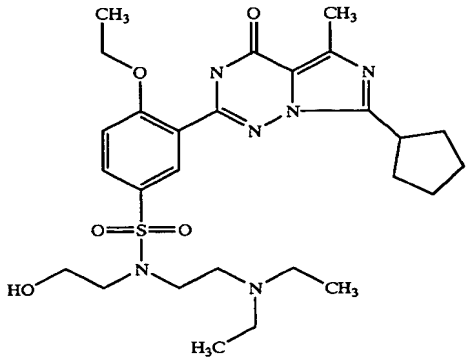
179		529.6	83
180		529.6	86
181		560.7	82

TABLE 1-continued

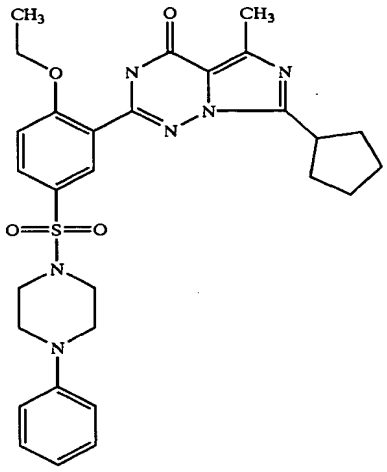
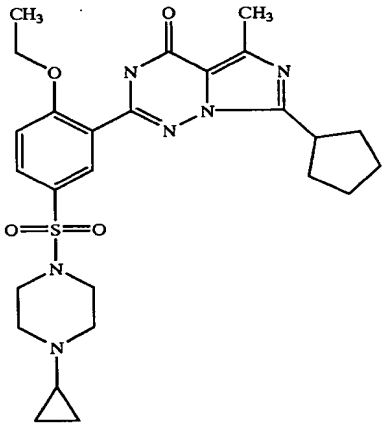
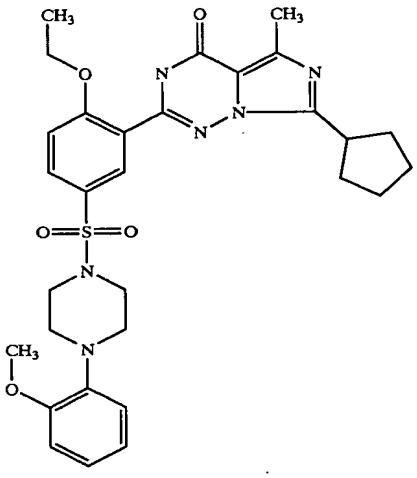
182		562.7	81
183		526.7	60
184		592.7	80

TABLE 1-continued

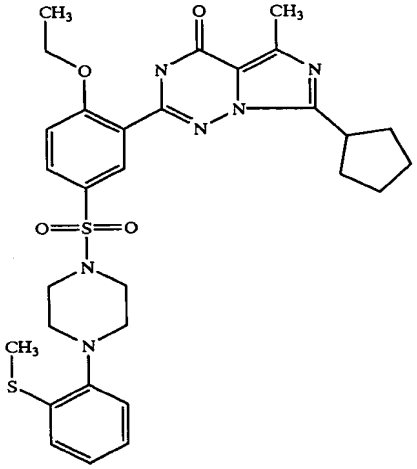
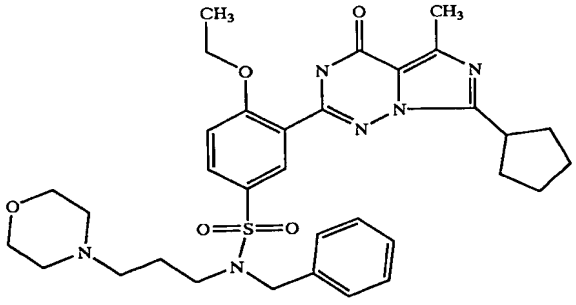
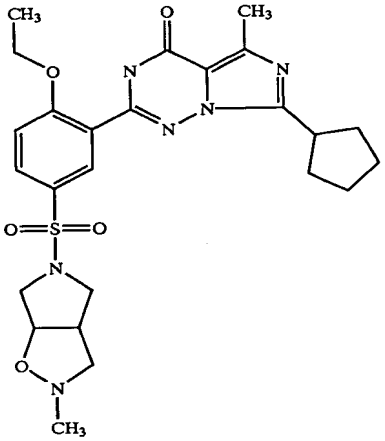
185		608.8	80
186		634.8	77
187		528.6	71

TABLE 1-continued

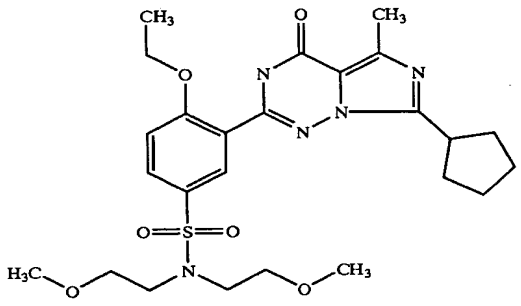
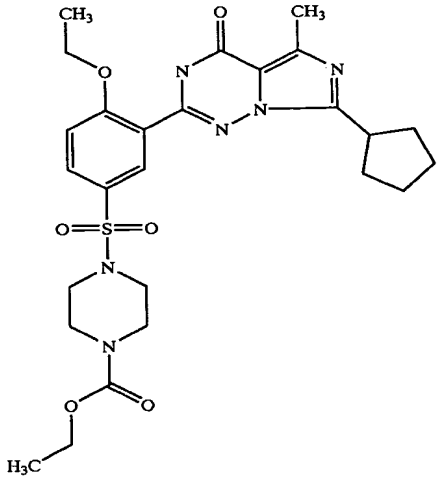
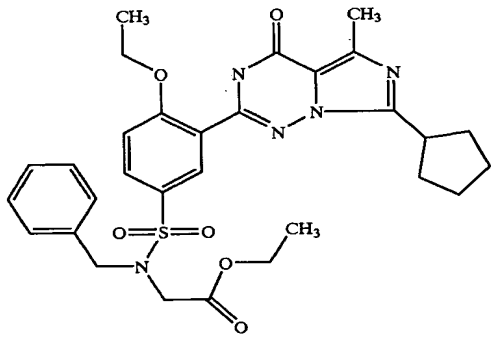
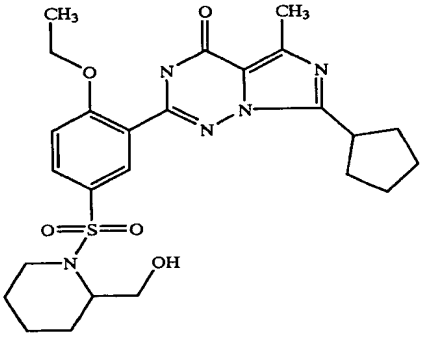
188		533.7	87
189		558.7	88
190		593.7	73
191		515.6	80

TABLE 1-continued

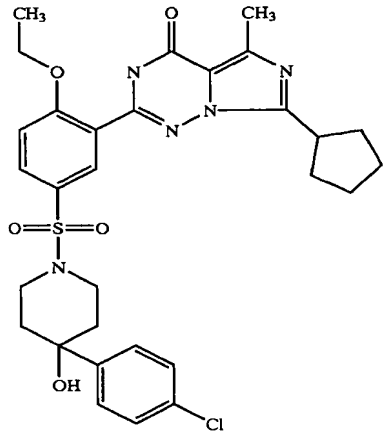
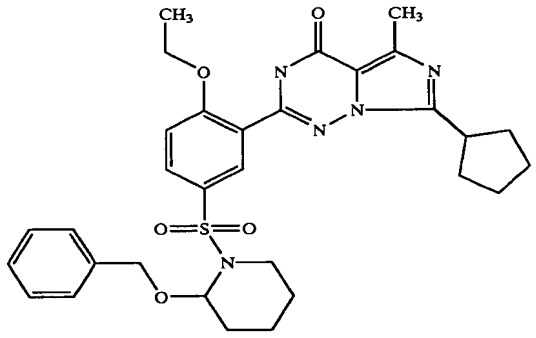
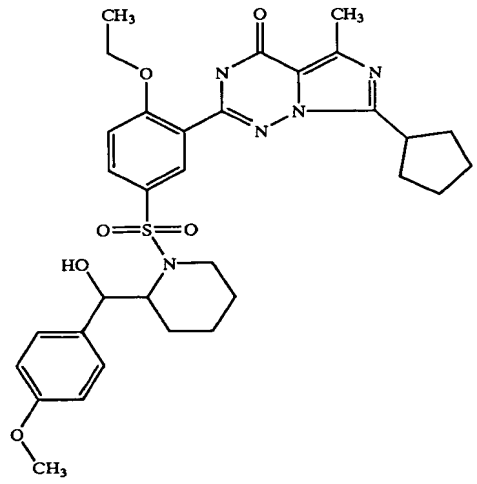
192		612.2	81
193		591.7	83
194		621.8	79

TABLE 1-continued

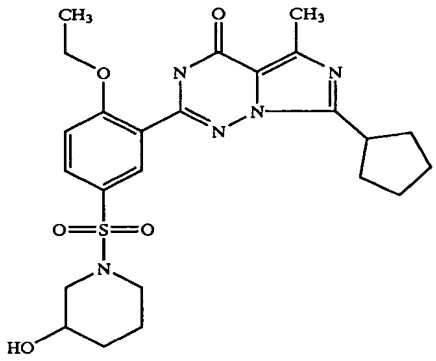
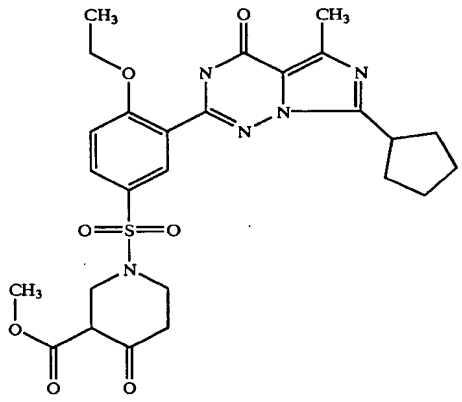
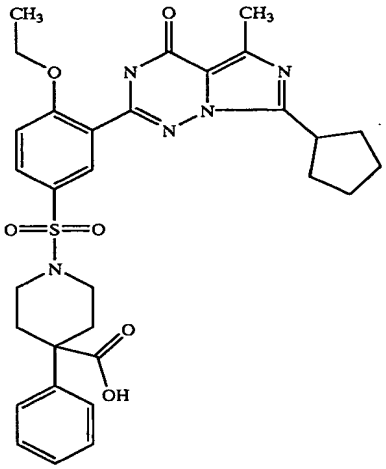
195		501.6	78
196		557.6	57
197		605.7	80

TABLE 1-continued

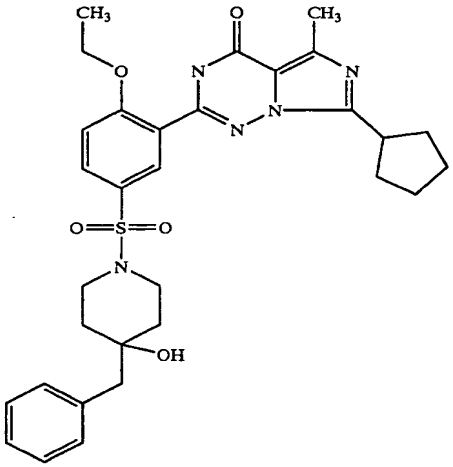
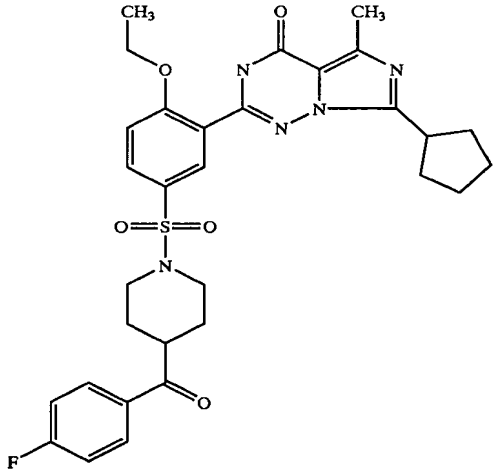
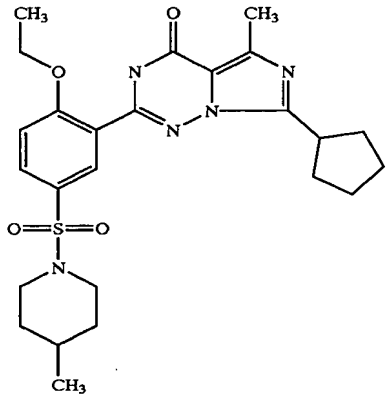
198		591.7	80
199		607.7	78
200		499.6	83

TABLE 1-continued

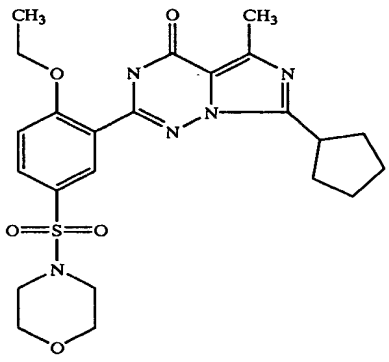
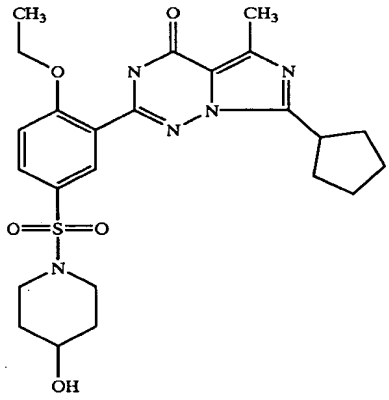
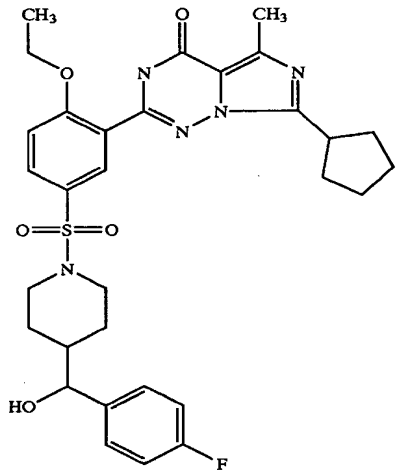
201		487.6	82
202		501.6	66
203		609.7	79

TABLE 1-continued

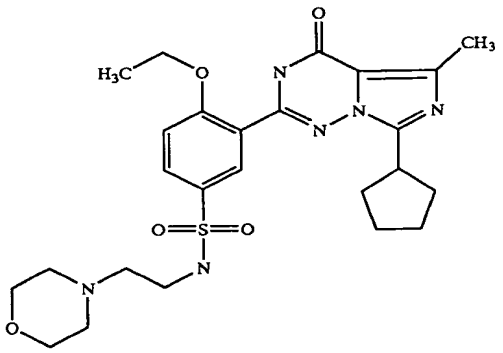
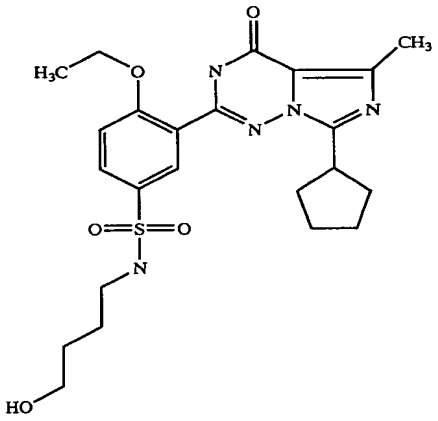
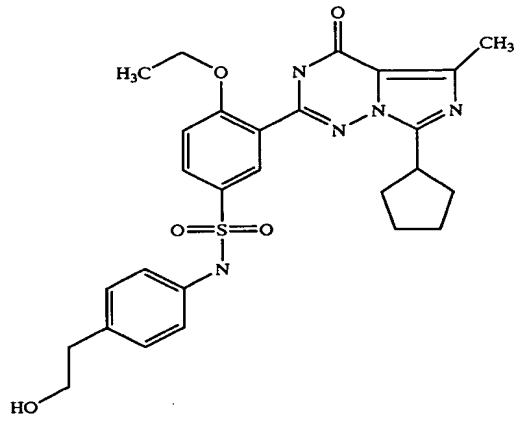
204		530.7	82
205		489.6	80
206		537.6	63

TABLE 1-continued

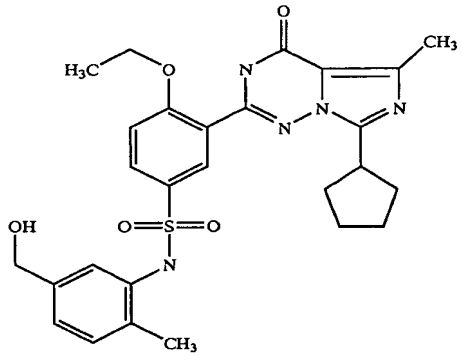
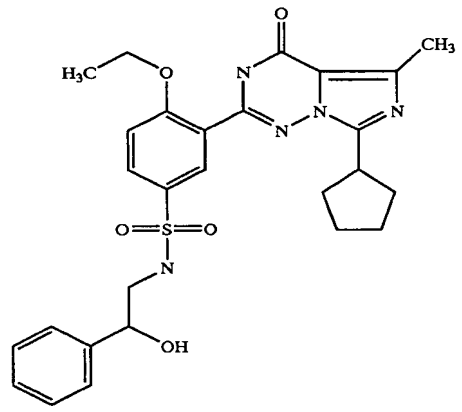
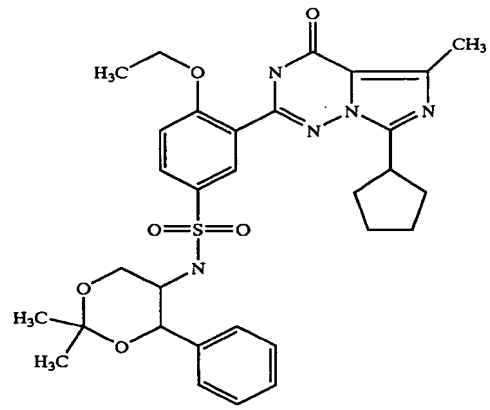
207		537.6	75
208		537.6	72
209		607.7	50

TABLE 1-continued

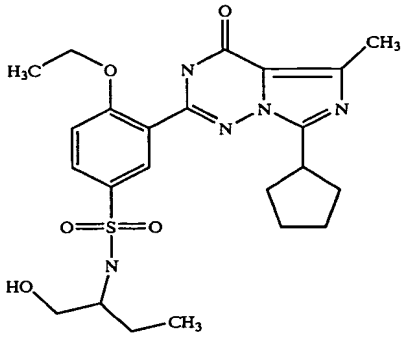
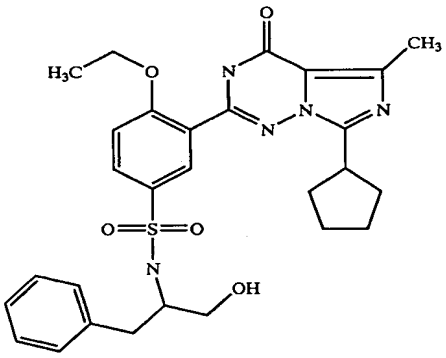
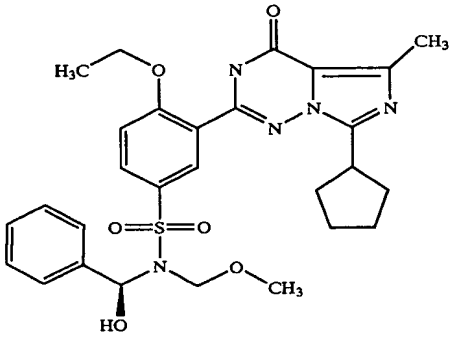
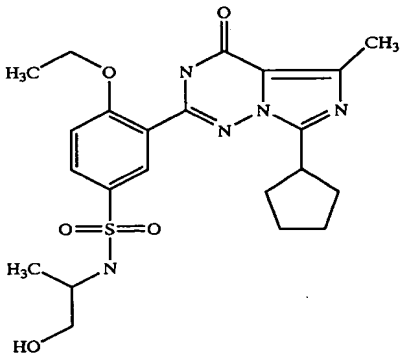
210		489.6	64
211		551.7	77
212		581.7	85
213		475.6	45

TABLE 1-continued

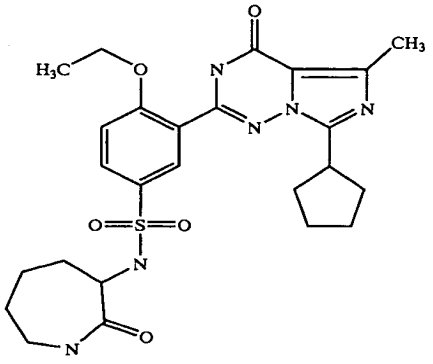
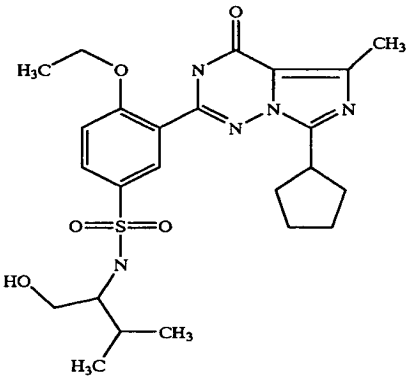
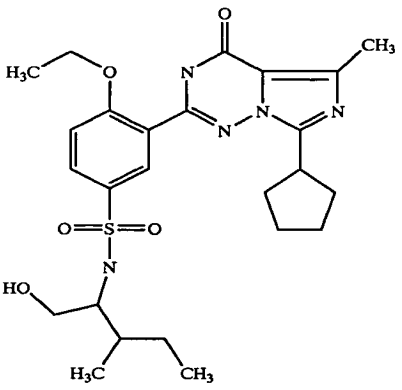
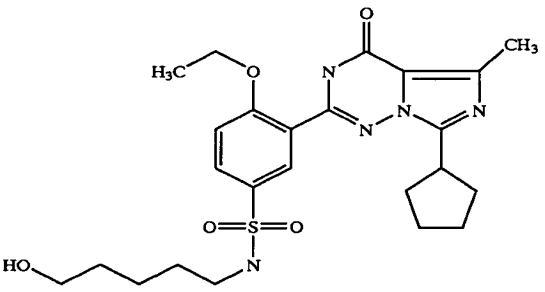
214		528.6	87
215		503.6	74
216		517.7	76
217		503.6	84

TABLE 1-continued

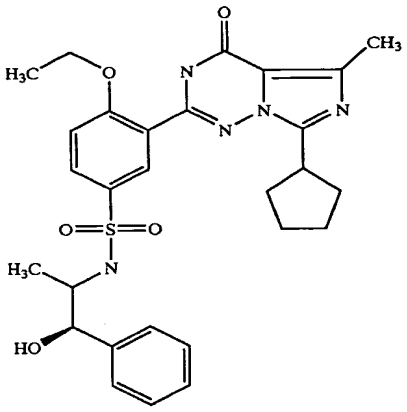
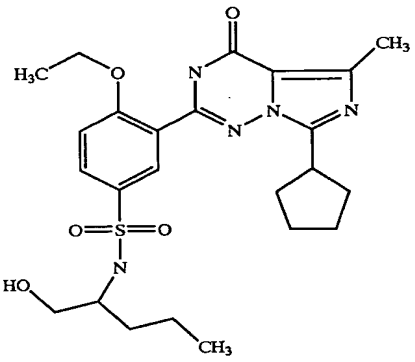
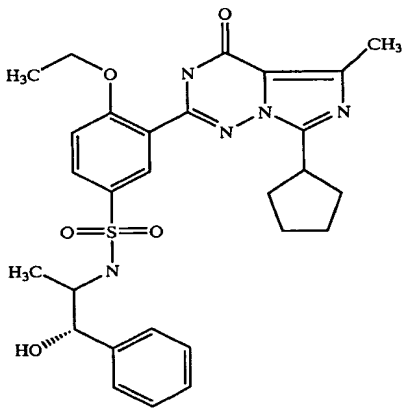
218		551.7	74
219		503.6	70
220		551.7	73

TABLE 1-continued

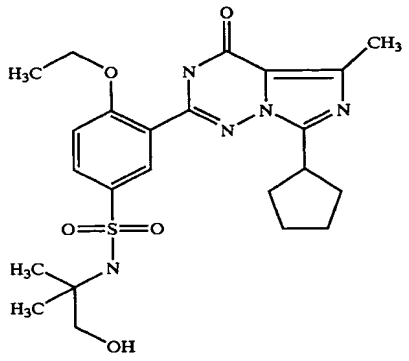
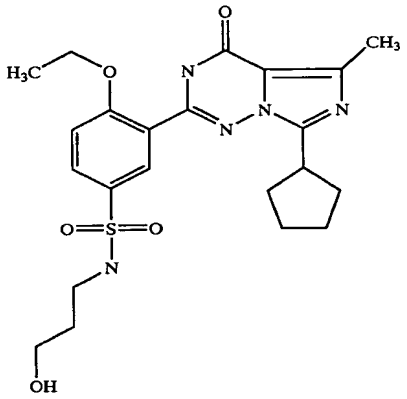
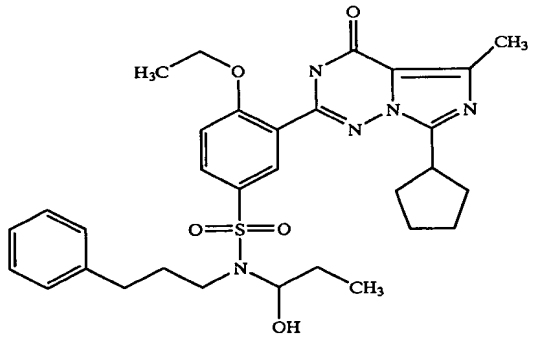
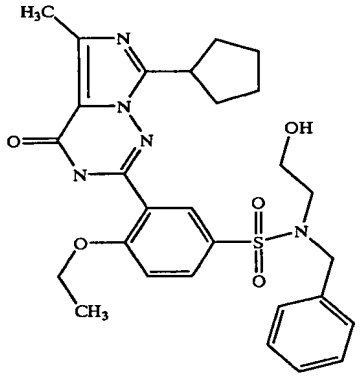
221		489.6	57
222		475.6	77
223		593.8	68
224		551.7	77

TABLE 1-continued

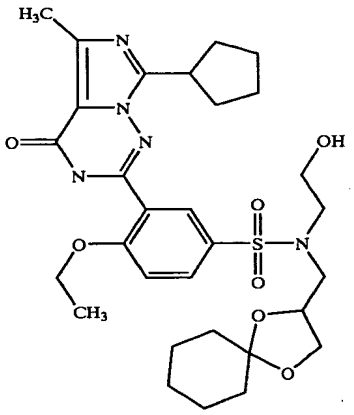
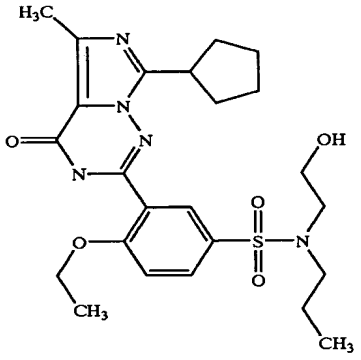
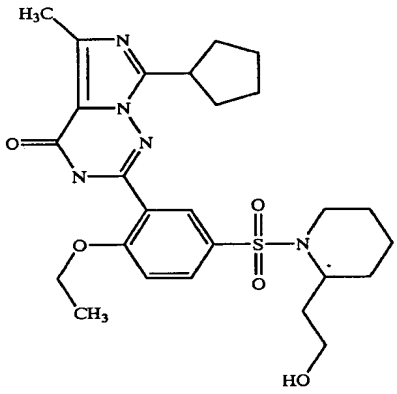
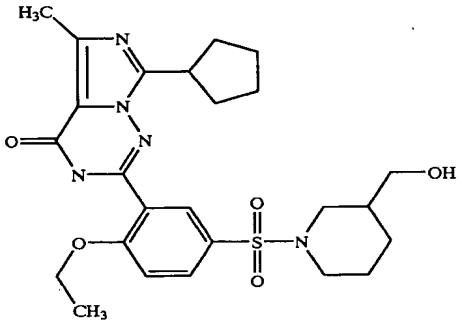
225		615.8	78
226		503.6	52
227		529.7	59
228		515.6	50

TABLE 1-continued

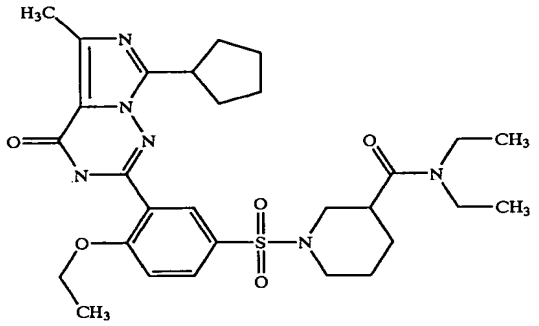
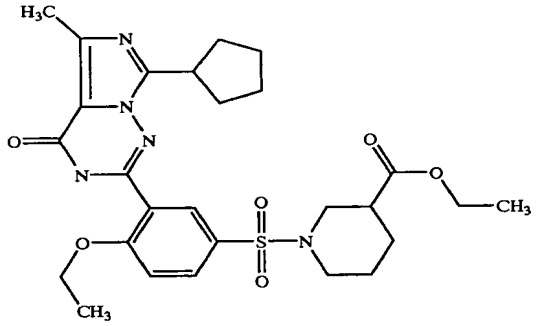
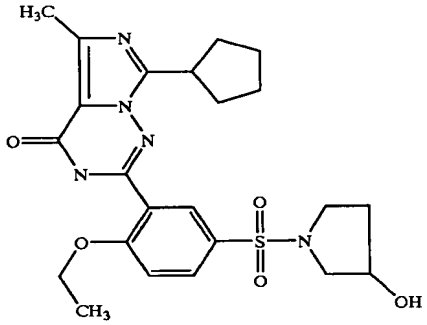
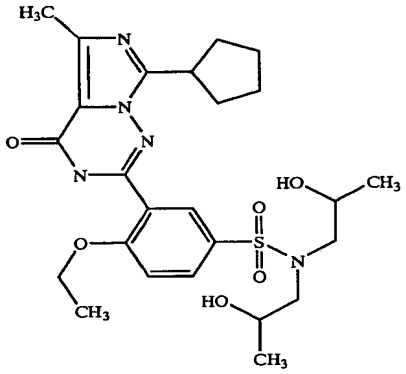
229		584.7	42
230		557.7	82
231		487.6	49
232		533.7	80

TABLE 1-continued

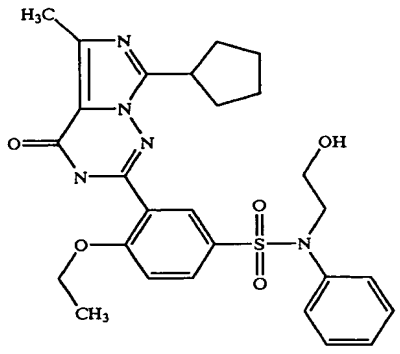
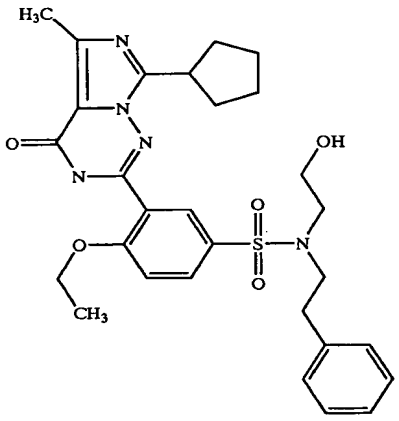
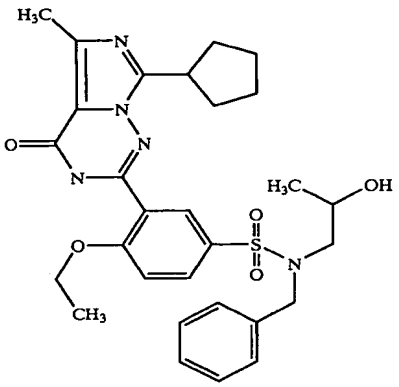
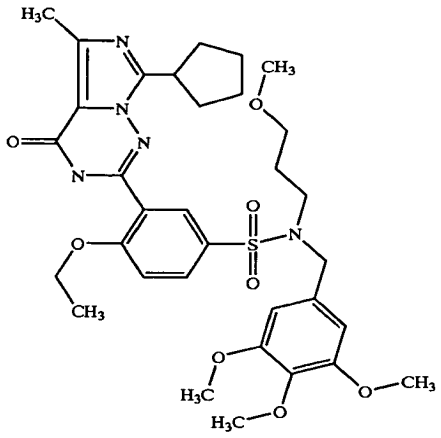
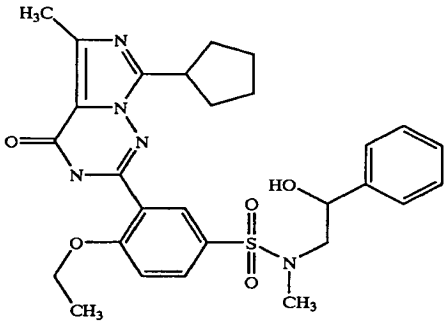
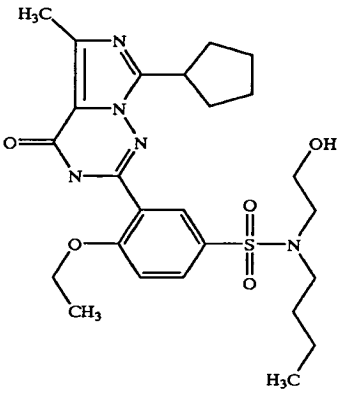
233		537.6	81
234		565.7	82
235		565.7	56

TABLE 1-continued

236		669.8	82
237		551.7	77
238		517.7	91

*The yields are based on the molecular peaks determined by mass spectroscopy.

TABLE 1-continued

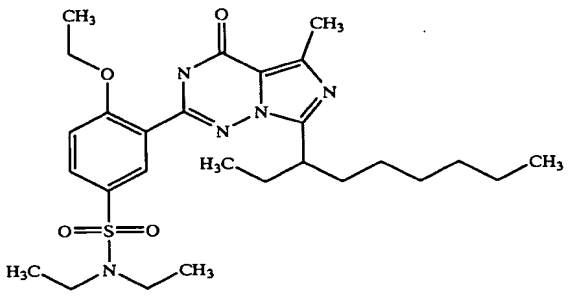
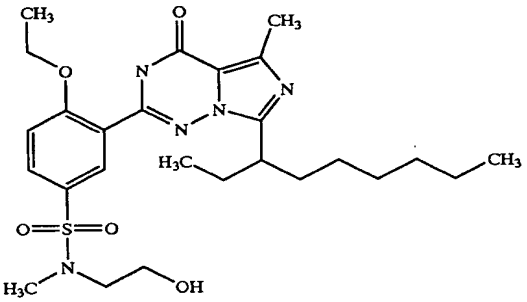
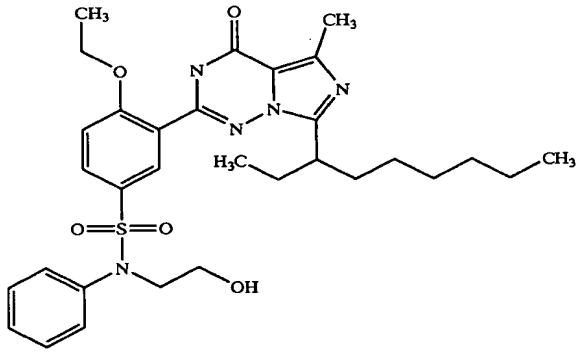
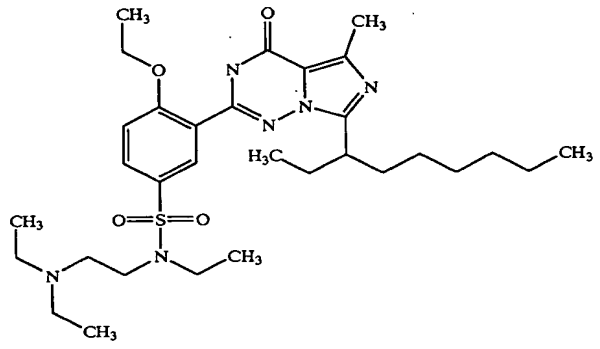
Ex. No.	Structure	MW [g/mol]	HPLC	Mz + H
239		531.723	77	532
240		533.695	71	534
241		595.767	65	596
242		602.846	53	603

TABLE 1-continued

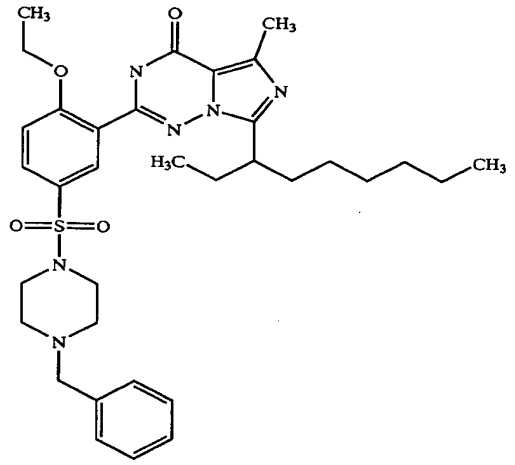
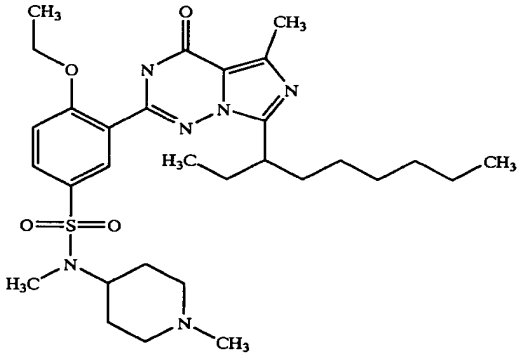
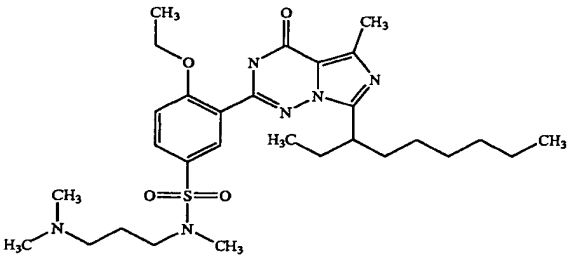
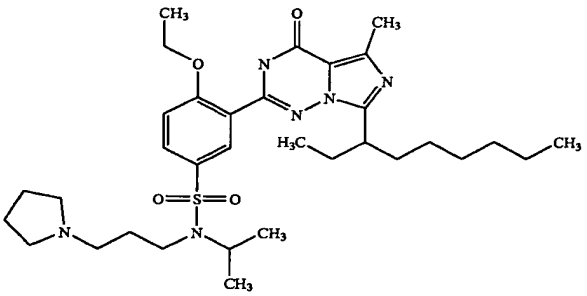
243		634.848	64	635
244		586.803	51	587
245		574.792	61	575
246		628.884	41	629

TABLE 1-continued

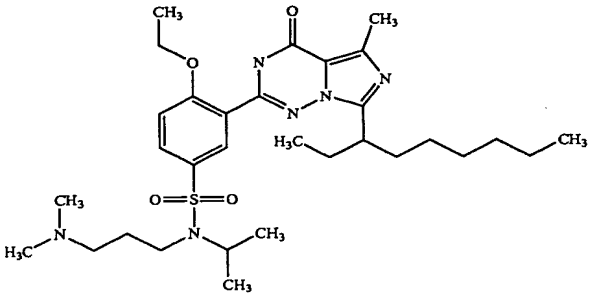
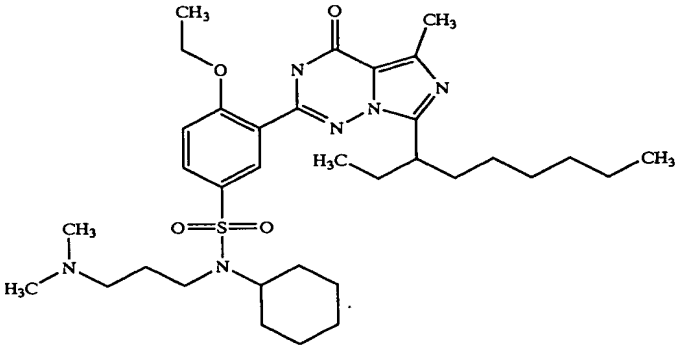
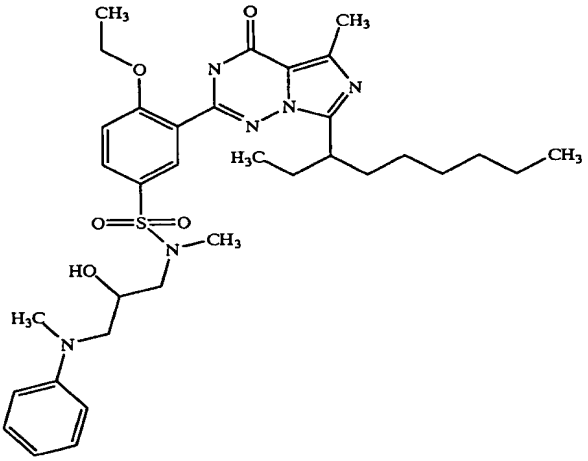
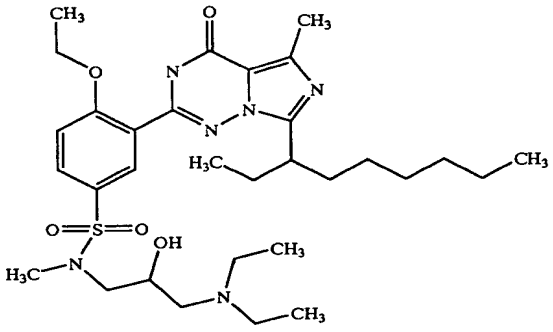
247		602.846	42	603
248		642.911	44	643
249		652.863	66	653
250		618.845	48	619

TABLE 1-continued

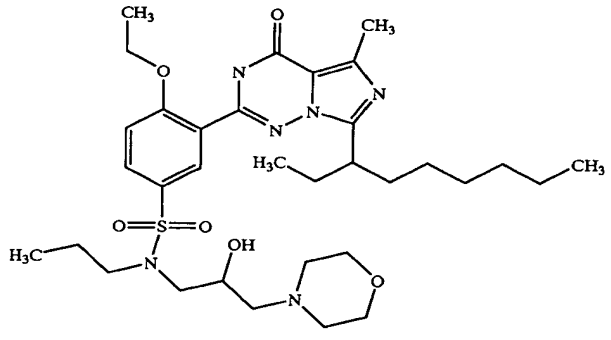
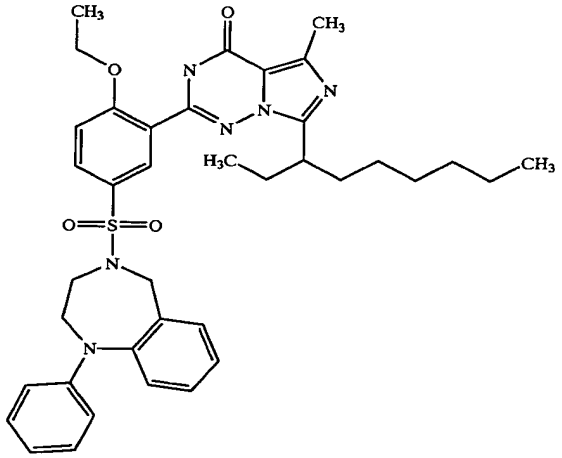
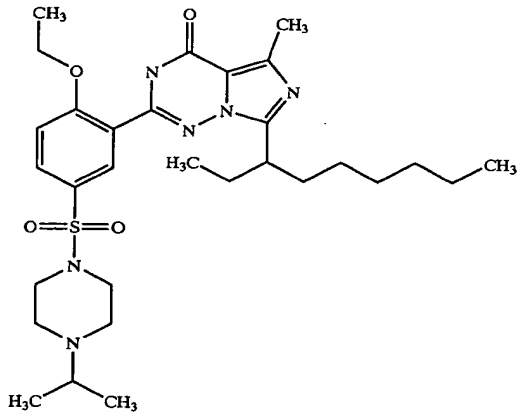
251		660.883	71	661
252		682.892	50	683
253		600.83	60	601

TABLE 1-continued

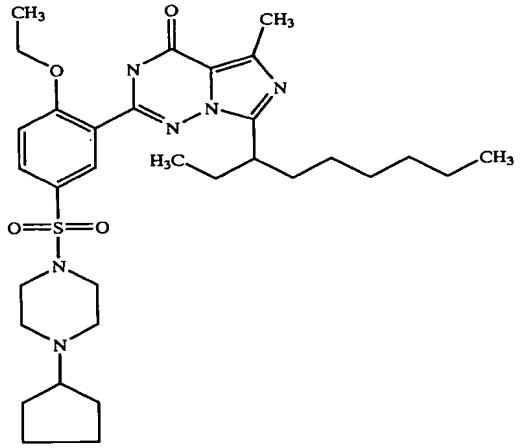
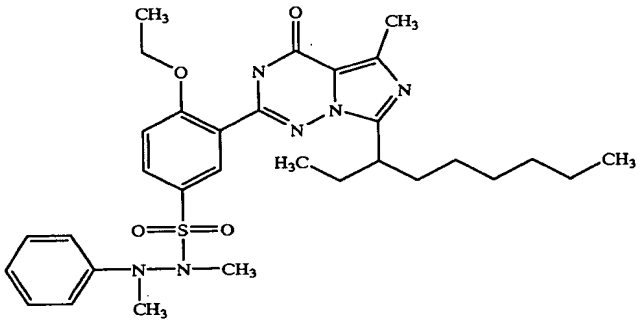
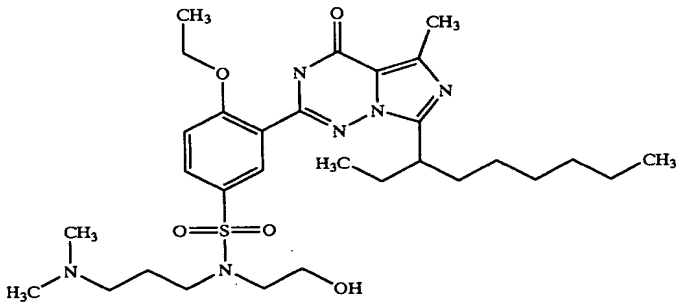
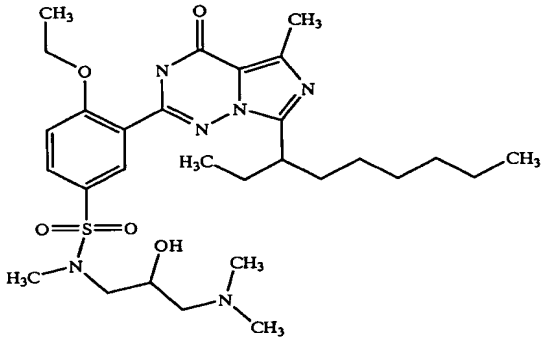
254		612.841	68	613
255		622.836	66	623
256		604.818	58	605
257		590.791	56	591

TABLE 1-continued

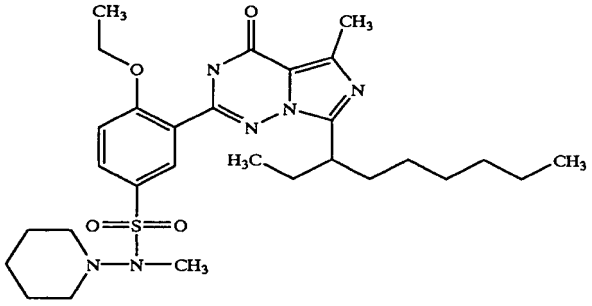
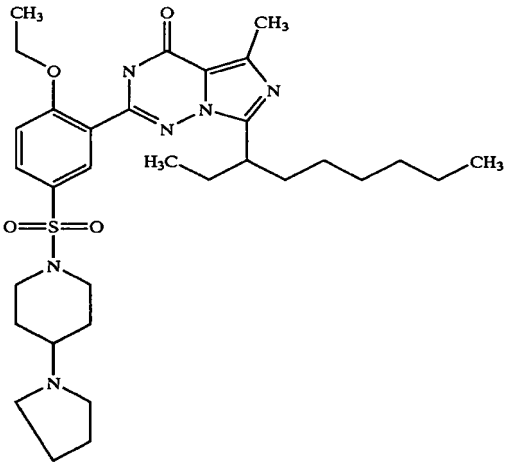
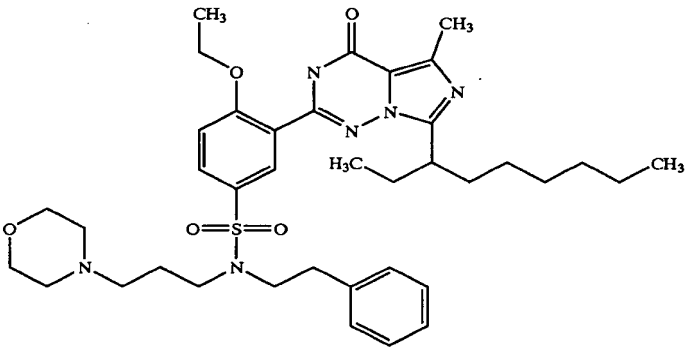
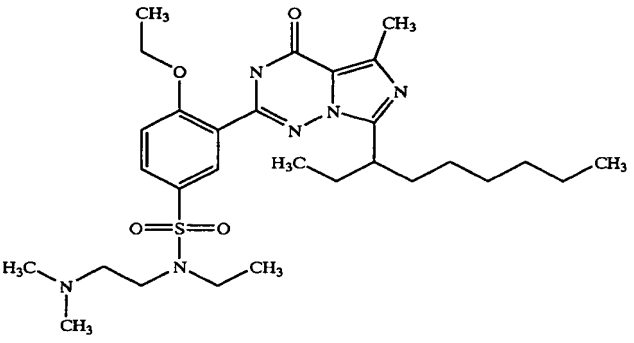
258		600.83	59	601
259		612.841	54	613
260		706.955	72	707
261		574.792	56	575

TABLE 1-continued

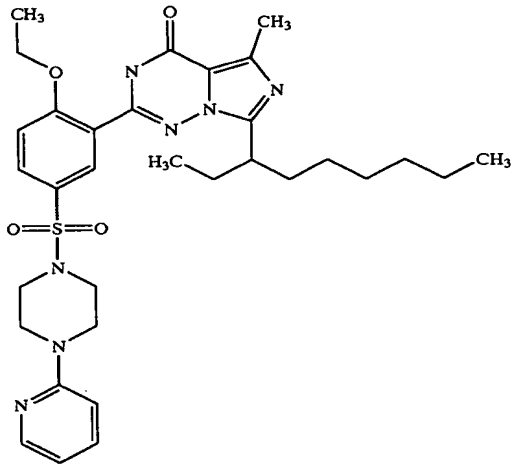
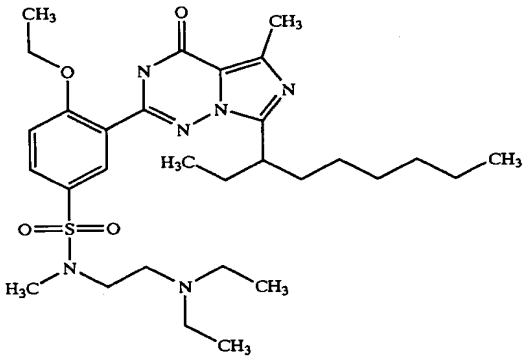
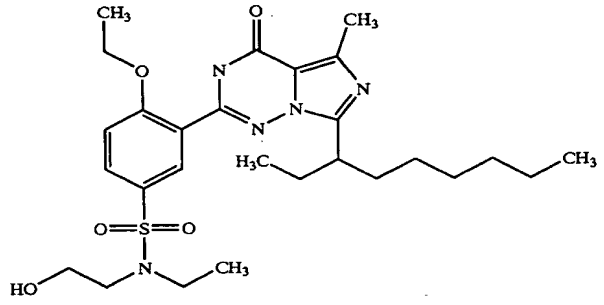
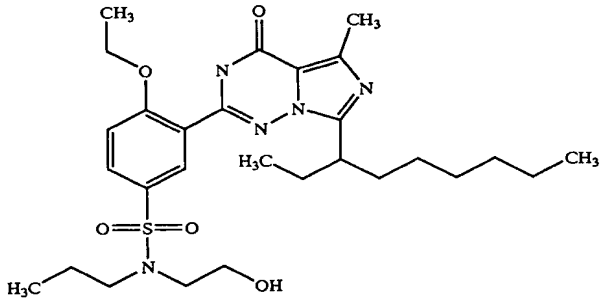
262		621.808	57	622
263		588.819	52	589
264		547.722	79	548
265		561.749	30	562

TABLE 1-continued

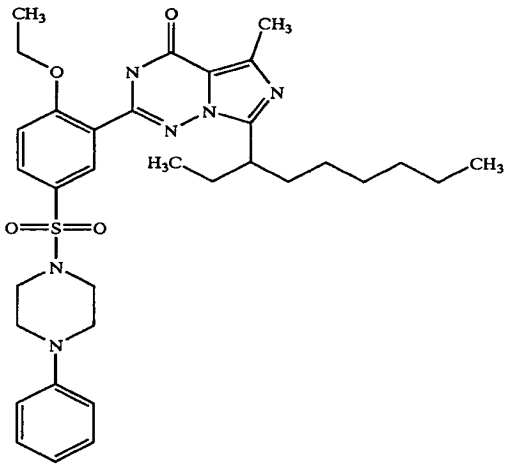
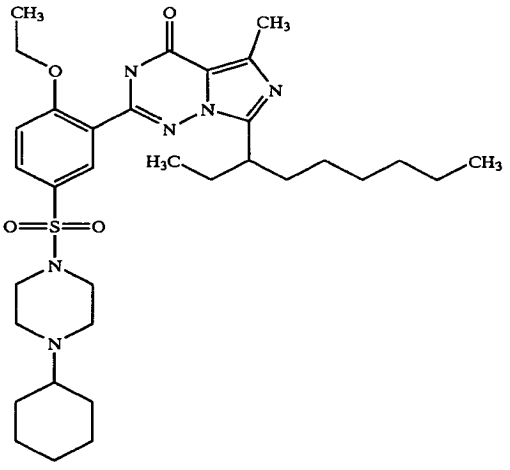
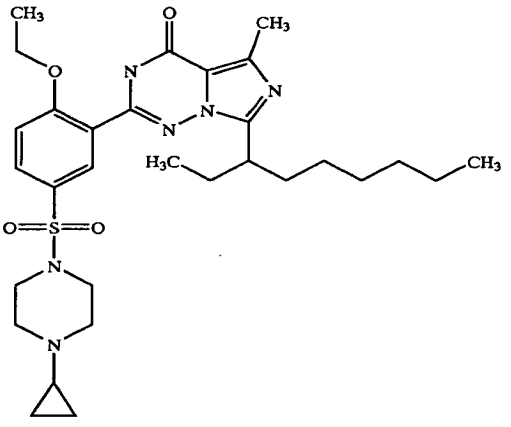
266		620.82	68	621
267		626.868	56	627
268		584.787	56	585

TABLE 1-continued

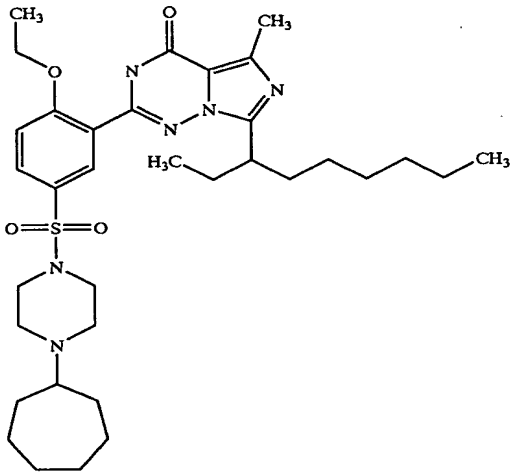
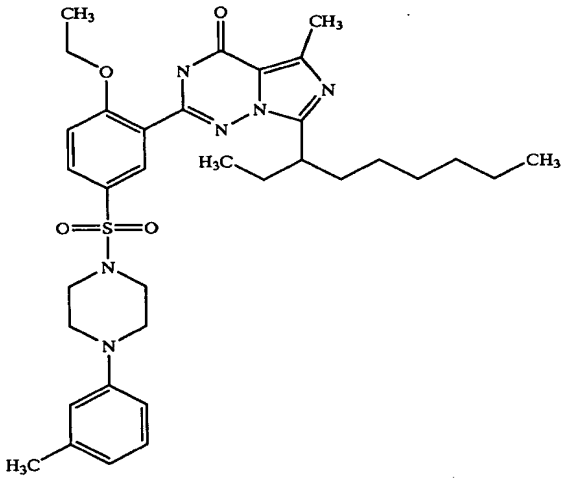
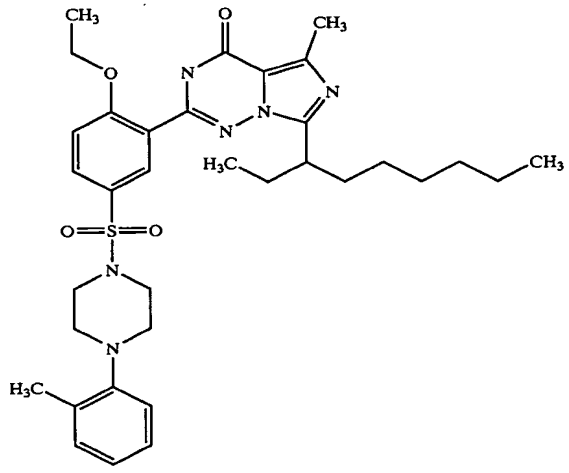
269		640.895	69	641
270		634.848	72	635
271		634.848	54	635

TABLE 1-continued

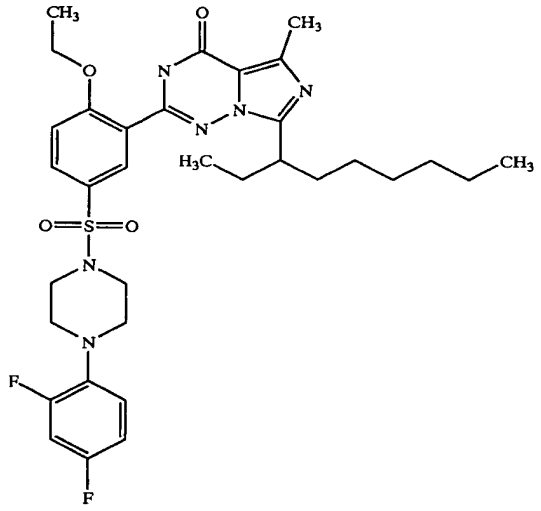
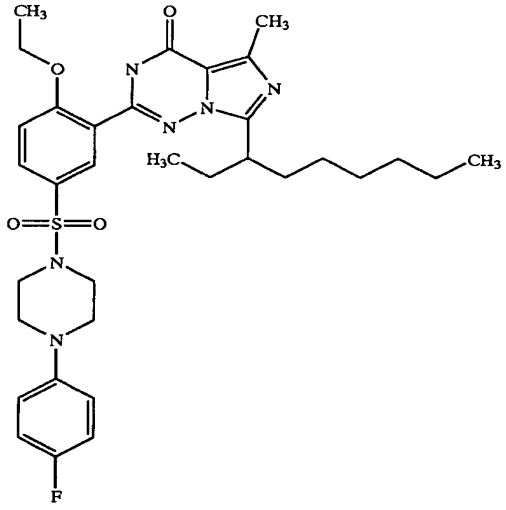
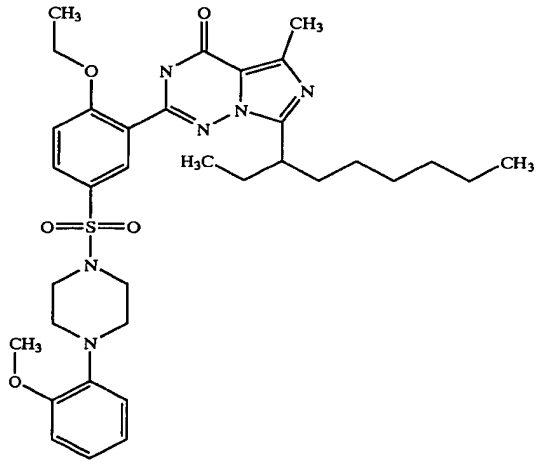
272		656.801	64	657
273		638.811	65	639
274		650.847	44	651

TABLE 1-continued

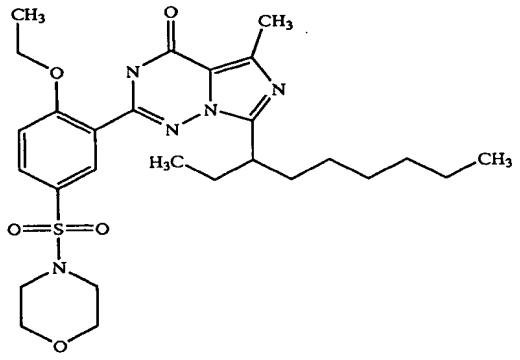
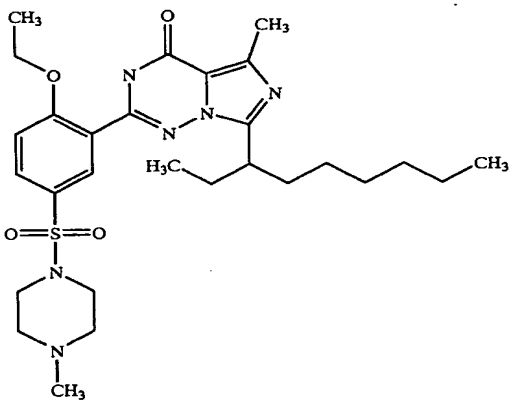
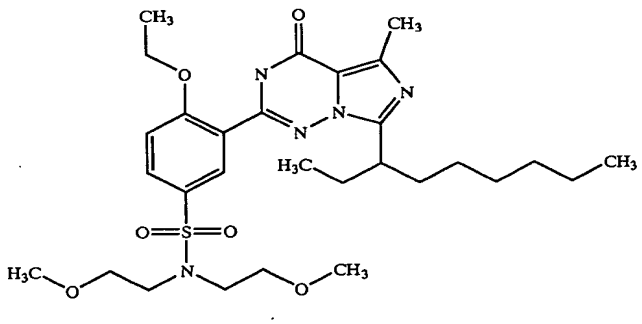
275		545.706	60	546
276		558.749	50	559
277		591.776	70	592

TABLE 1-continued

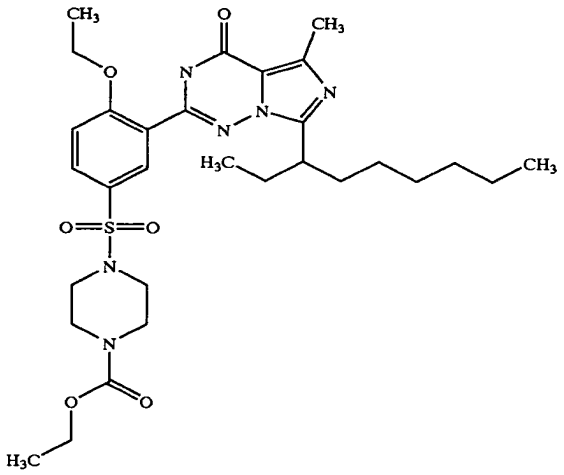
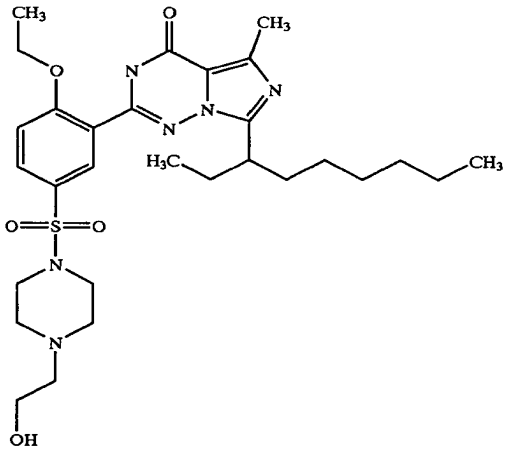
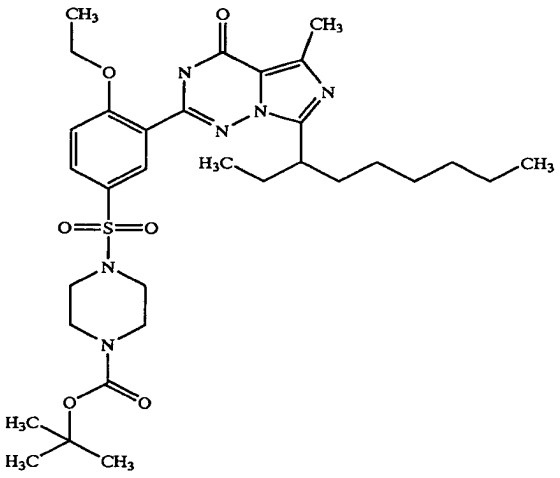
278		616.786	53	617
279		588.775	49	589
280		644.84	51	645

TABLE 1-continued

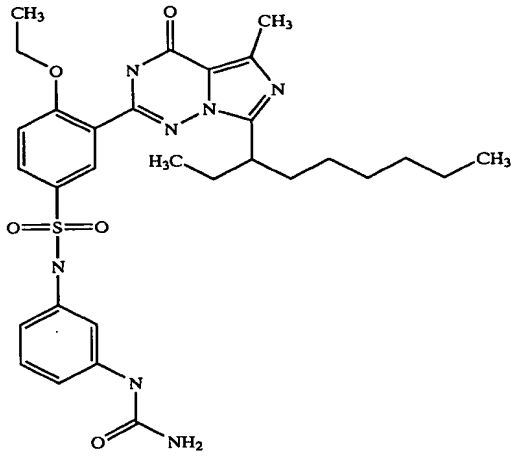
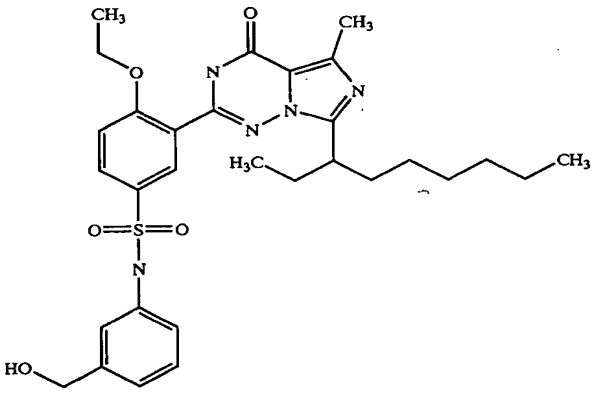
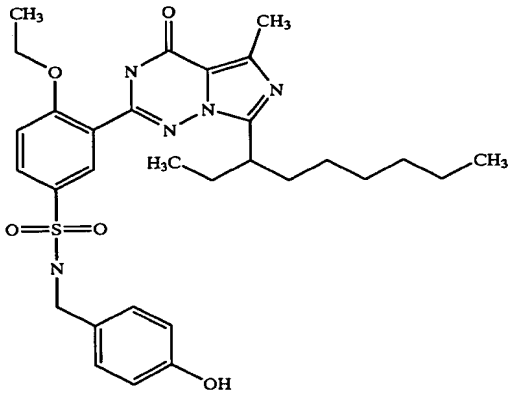
281		609.75323	55	610
282		581.73983	66	582
283		581.73983	63	582

TABLE 1-continued

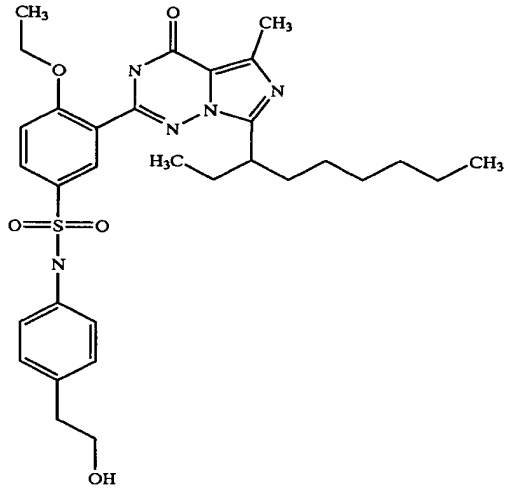
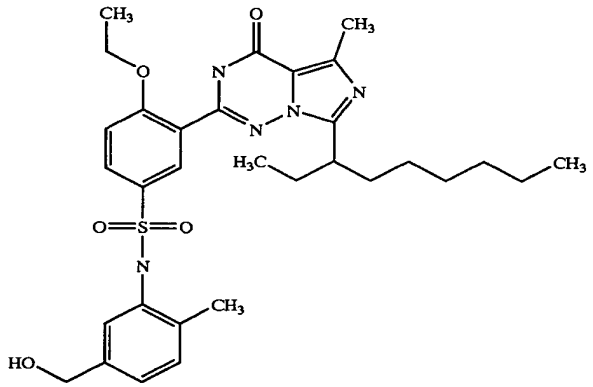
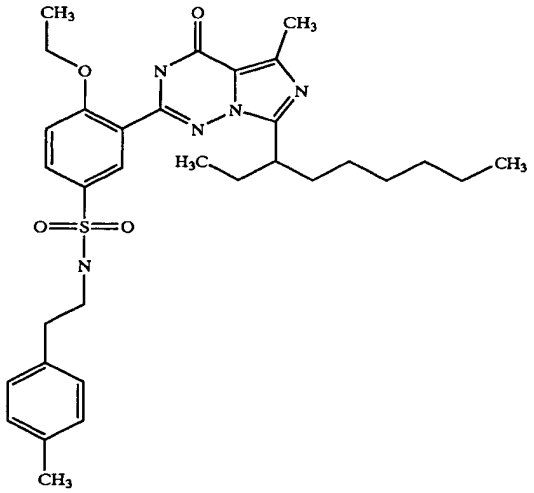
284		595.76692	68	596
285		5.76692	68	596
286		593.79461	70	594

TABLE 1-continued

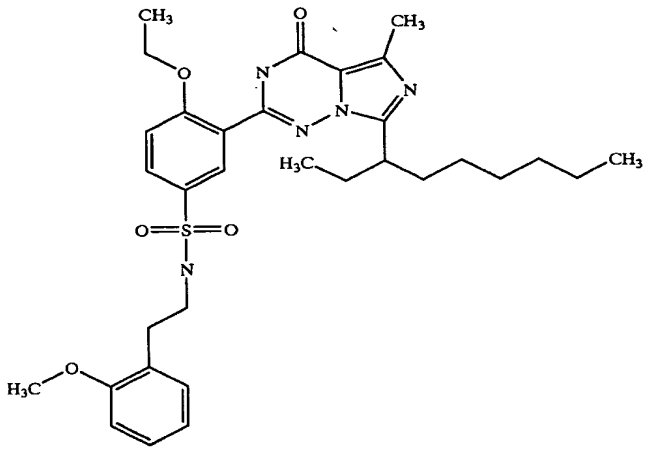
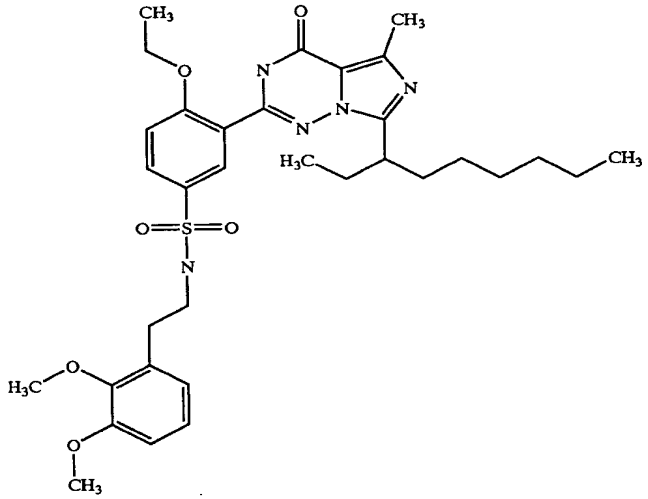
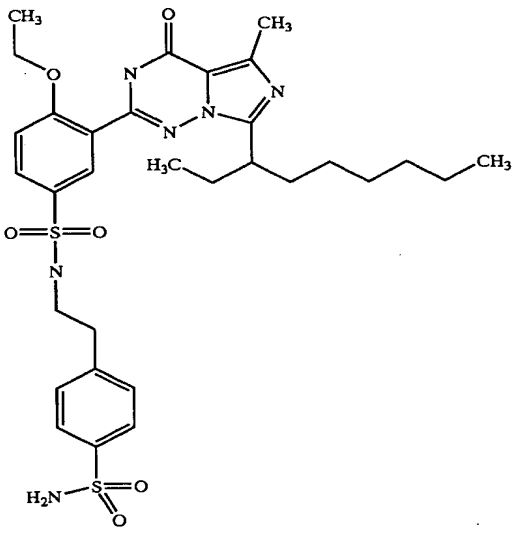
287		609.79401	68	610
288		639.8205	63	640
289		658.84499	61	659

TABLE 1-continued

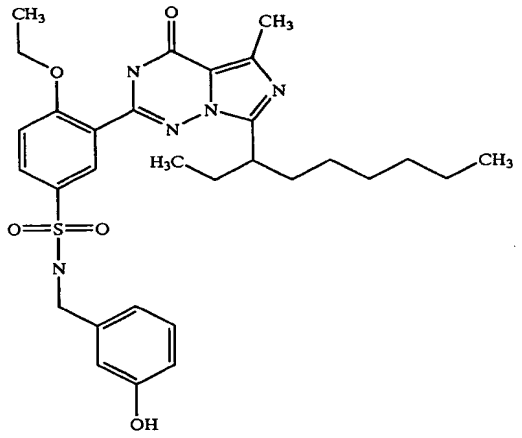
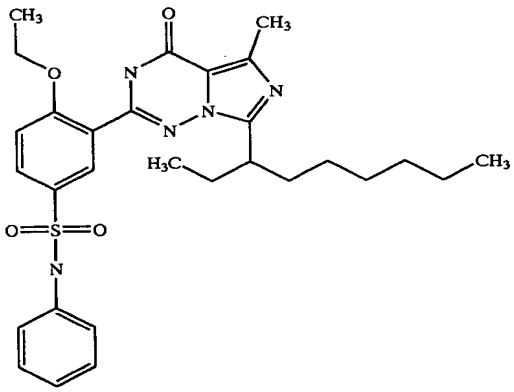
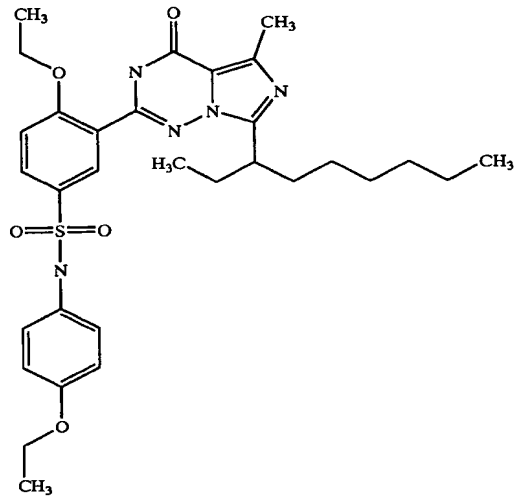
290		581.73983	59	582
291		551.71334	71	552
292		595.76692	69	596

TABLE 1-continued

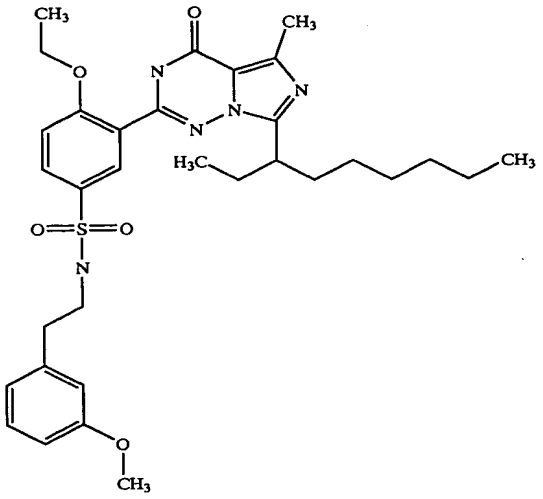
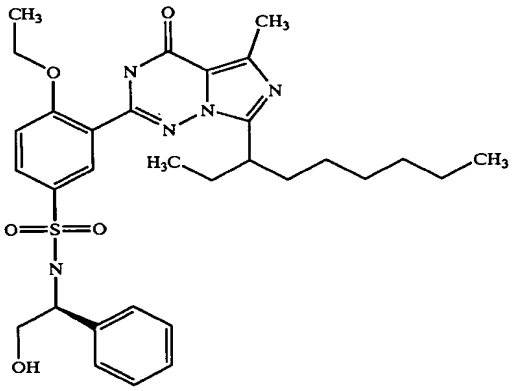
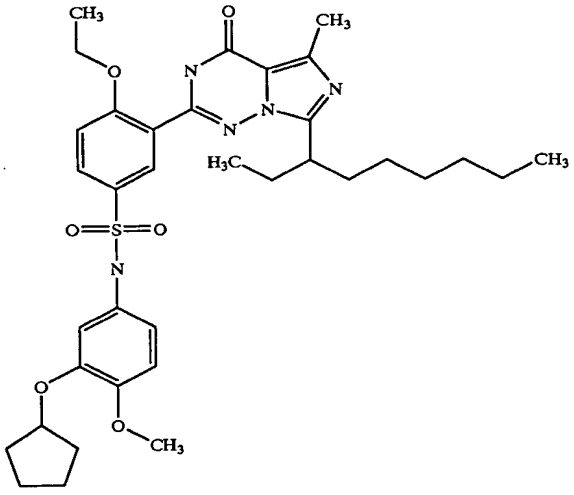
293		609.79401	65	610
294		595.76692	56	596
295		665.85874	54	666

TABLE 1-continued

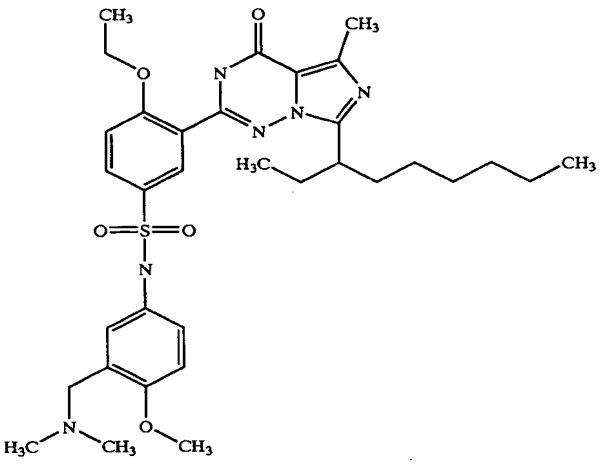
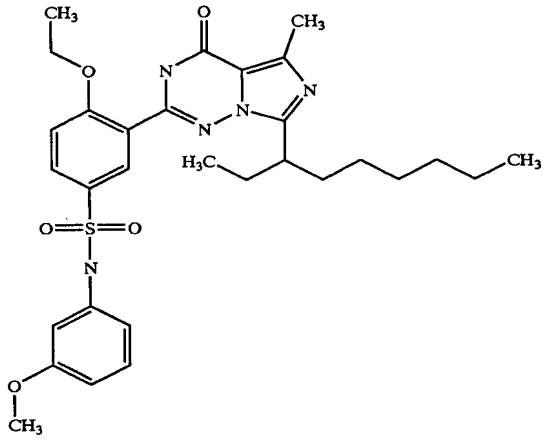
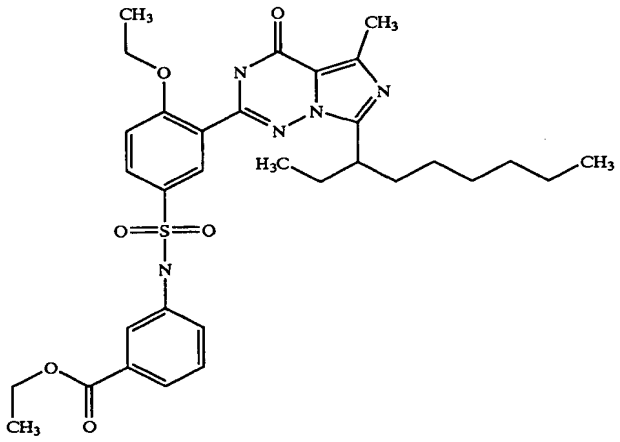
296		638.83577	64	639
297		581.73983	66	582
298		623.77747	63	624

TABLE 1-continued

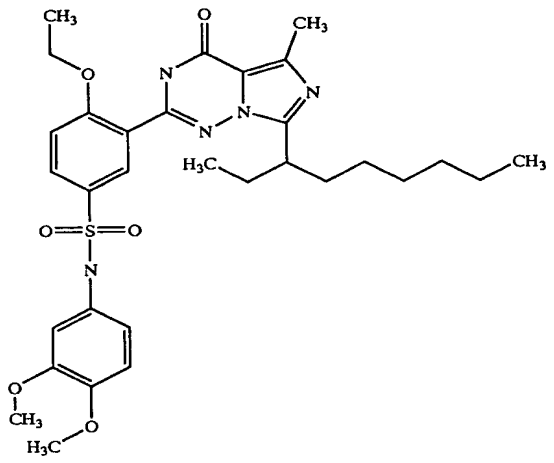
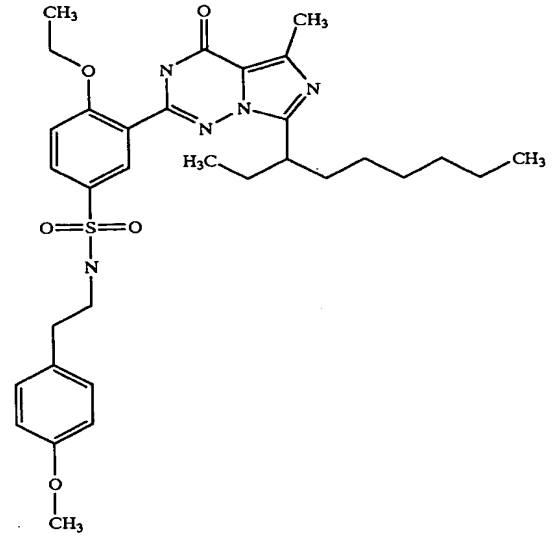
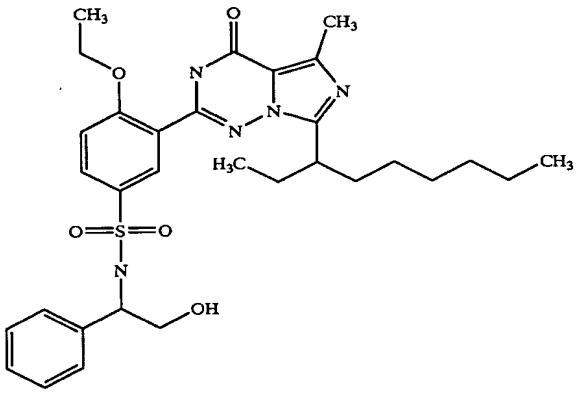
299		611.76632	65	612
300		609.79401	61	610
301		595.76692	65	596

TABLE 1-continued

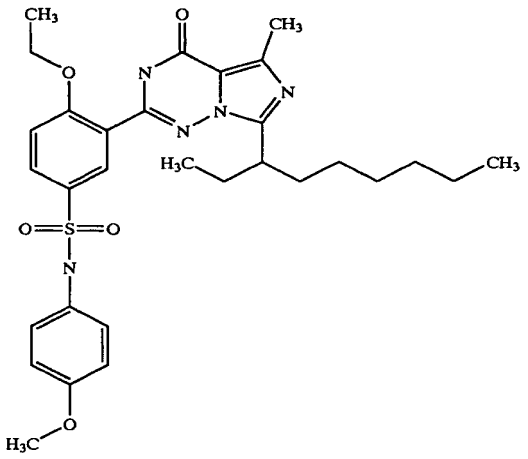
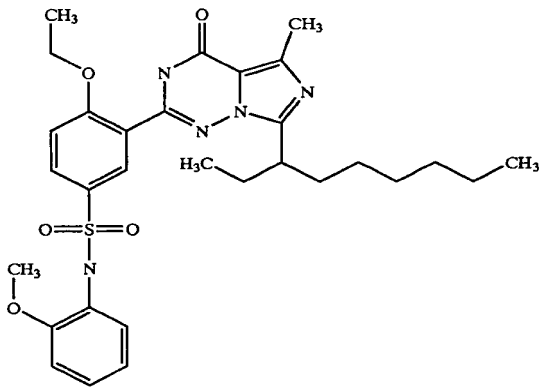
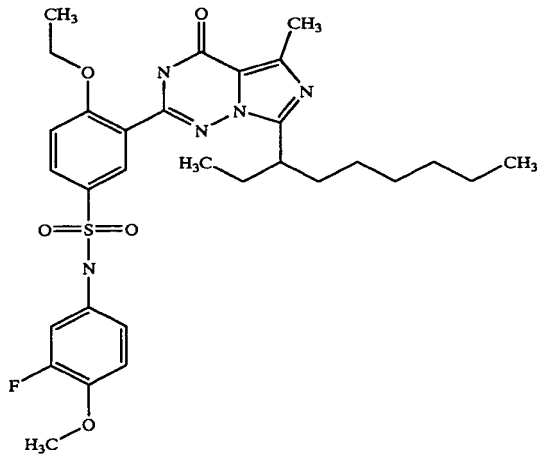
302		581.73983	71	582
303		581.73983	72	582
304		599.73026	69	600

TABLE 1-continued

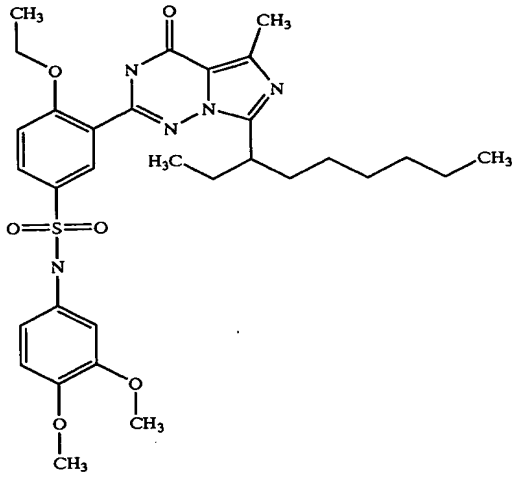
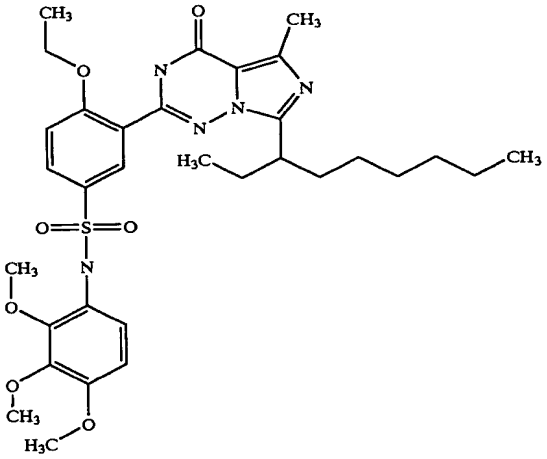
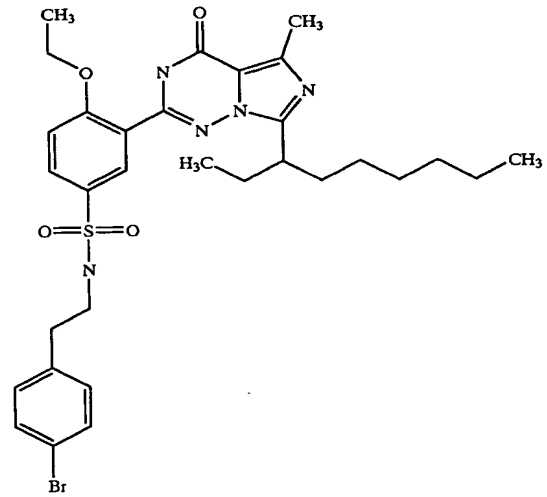
305		639.8205	65	640
306		641.79281	68	642
307		658.66355	75	658

TABLE 1-continued

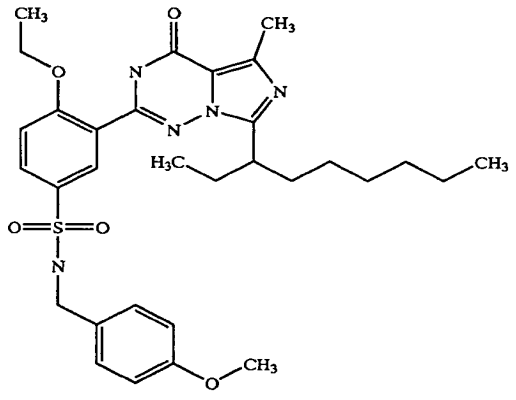
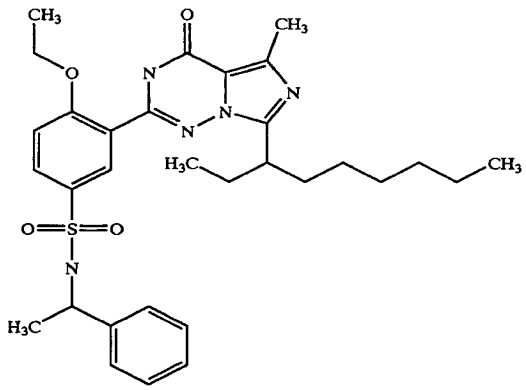
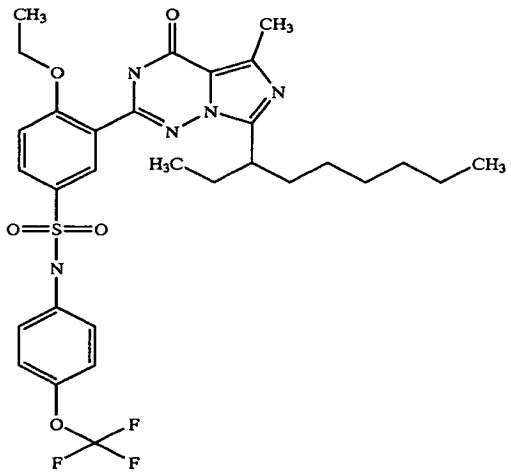
308		595.76692	72	596
309		579.76752	74	580
310		635.71112	69	636

TABLE 1-continued

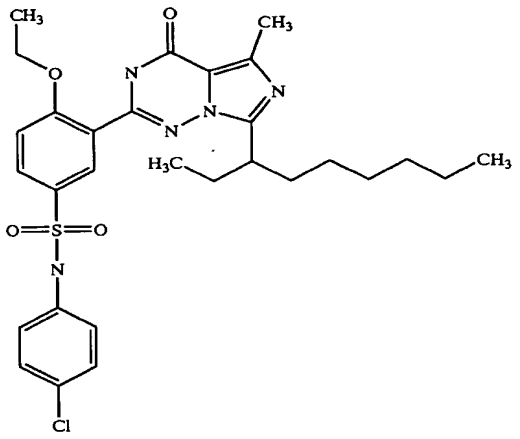
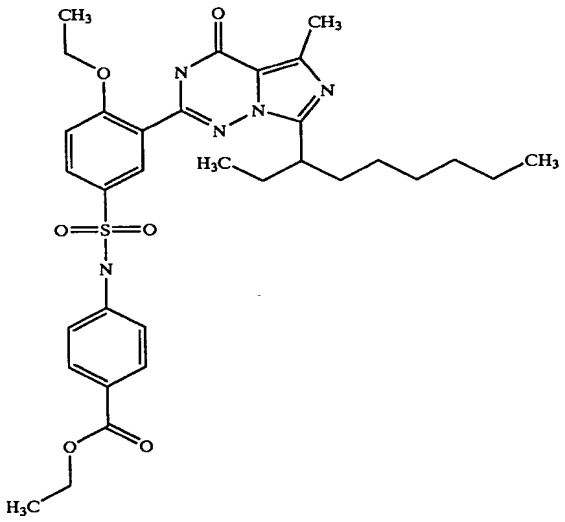
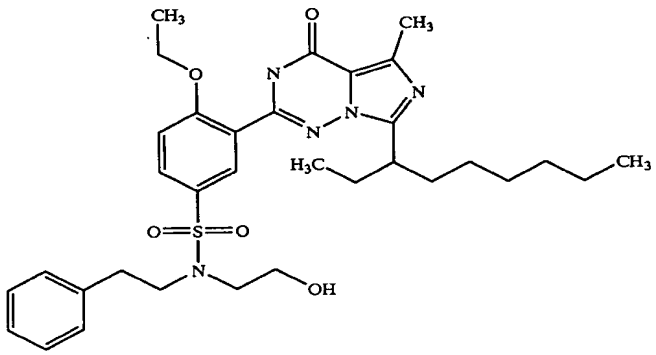
311		586.15837	64	586
312		623.77747	55	624
313.		623.8211	69	624

TABLE 1-continued

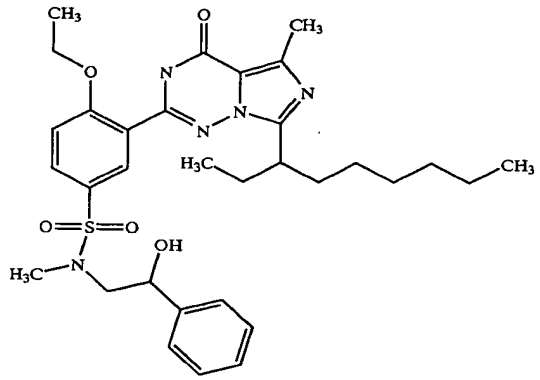
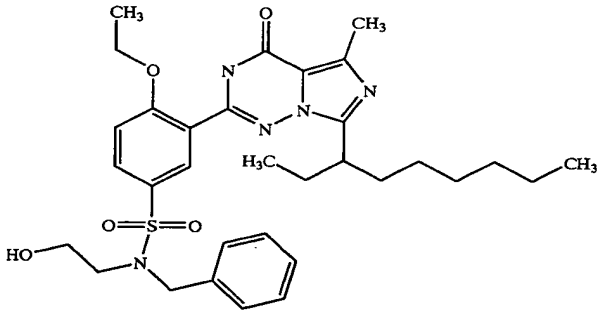
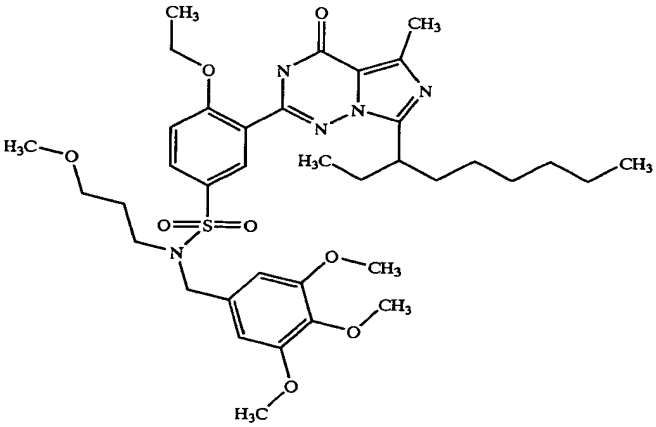
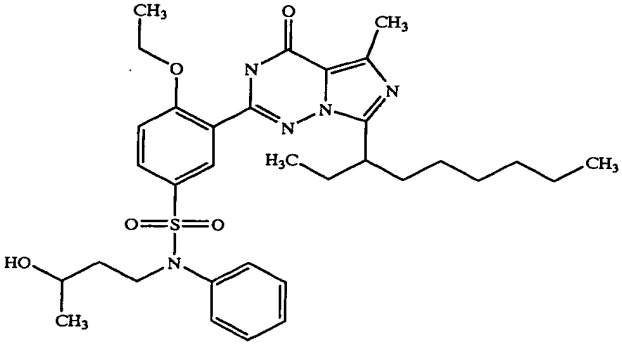
314		609.79401	72	610
315		609.79401	72	610
316		727.92766	65	728
317		623.8211	54	624

TABLE 1-continued

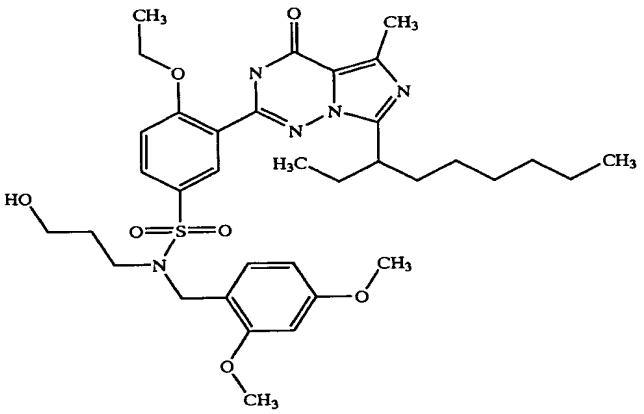
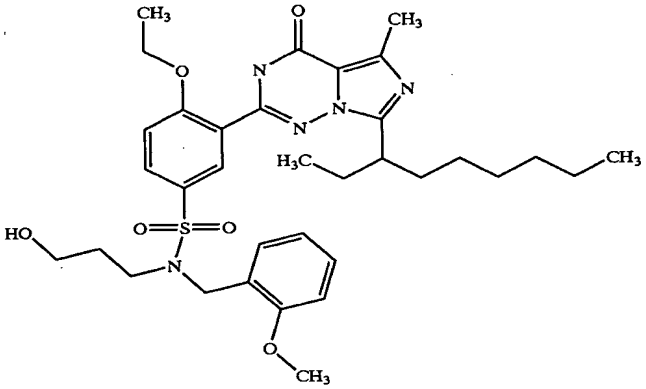
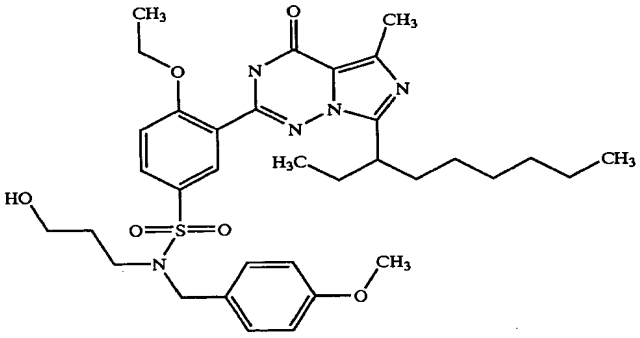
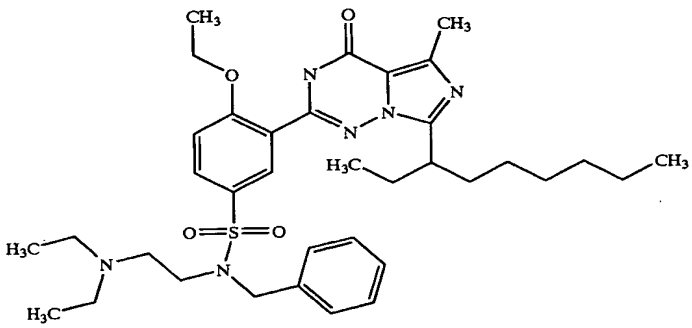
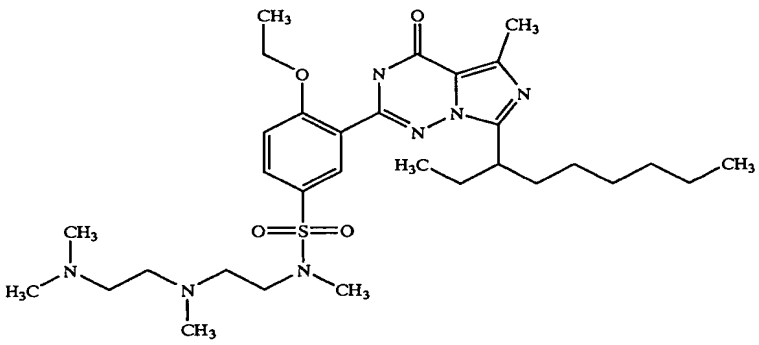
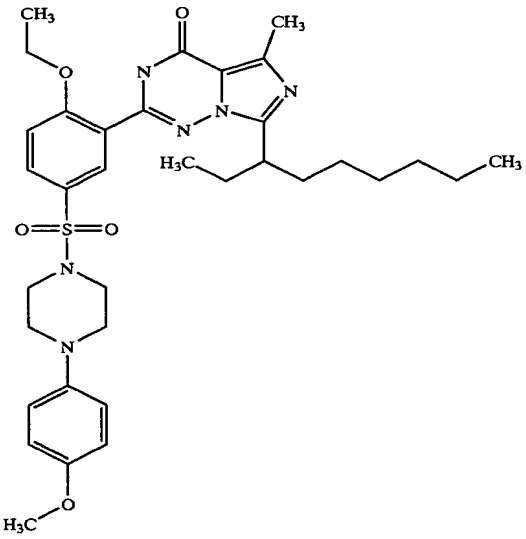
318		683.87408	68	684
319		653.84759	71	654
320		653.84759	68	654
321		664.91764	84	665

TABLE 1-continued

322		617.86062	60	618
323		650.84692	62	651

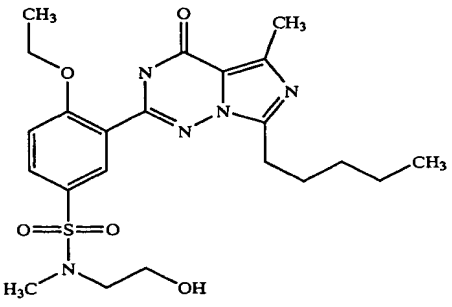
Ex. No.	Structure	MW [g/mol]	HPLC area % at 210 nm	Mz + H
324		477.5869	87	478

TABLE 1-continued

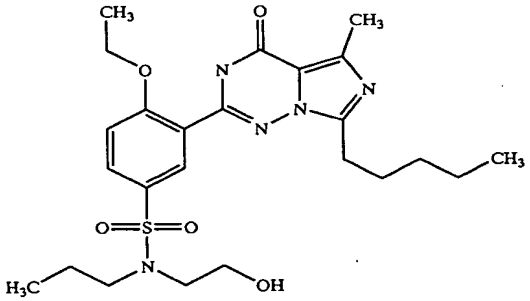
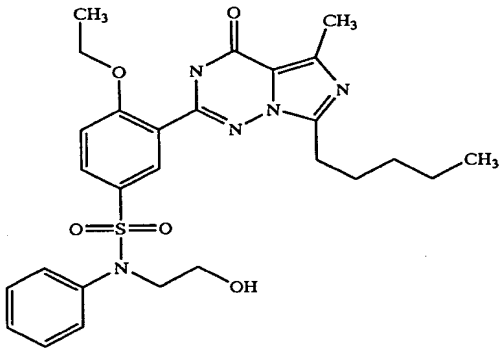
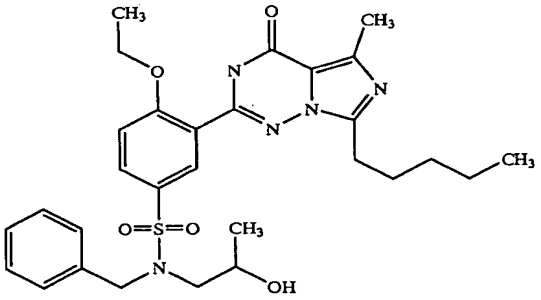
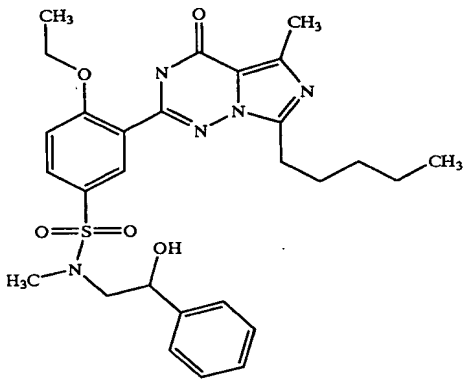
325		505.6411	89	506
326		539.6586	88	540
327		567.7127	81	566
328		553.6857	81	554

TABLE 1-continued

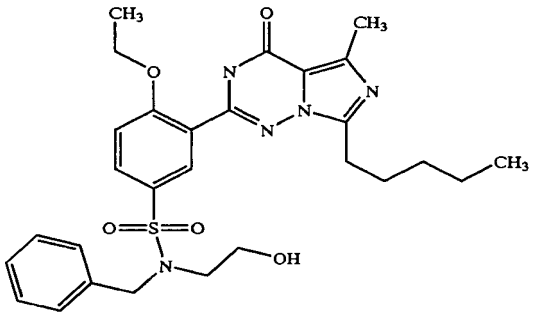
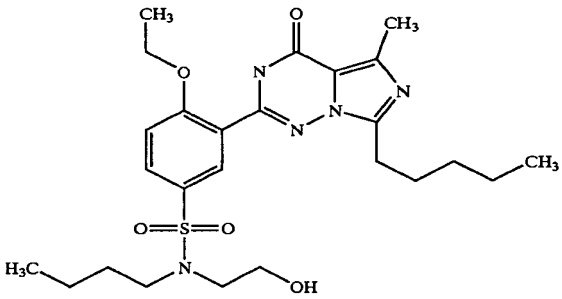
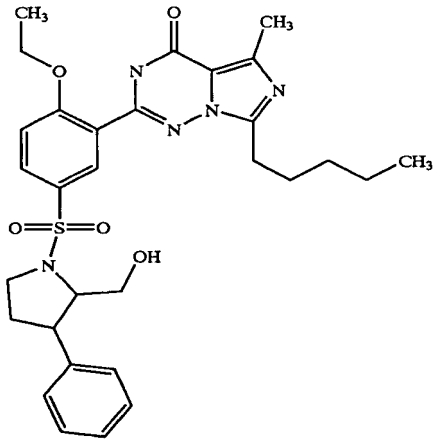
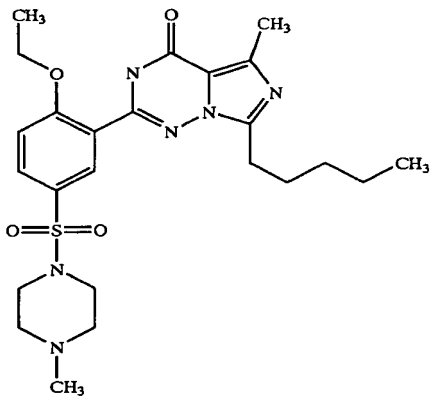
329		553.6857	83	554
330		519.6681	93	520
331		579.7239	77	580
332		502.6404	86	503

TABLE 1-continued

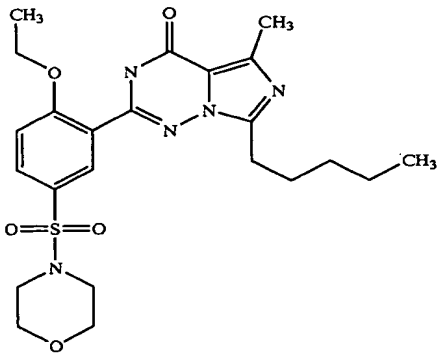
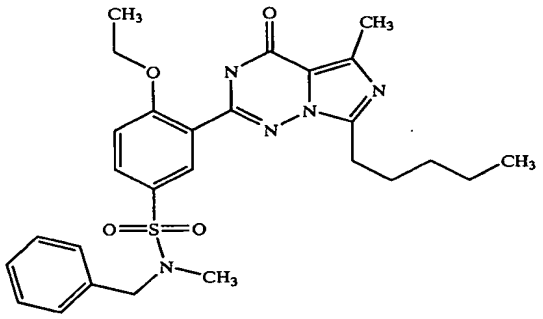
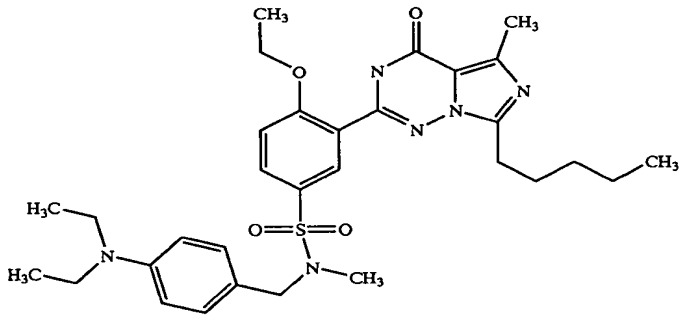
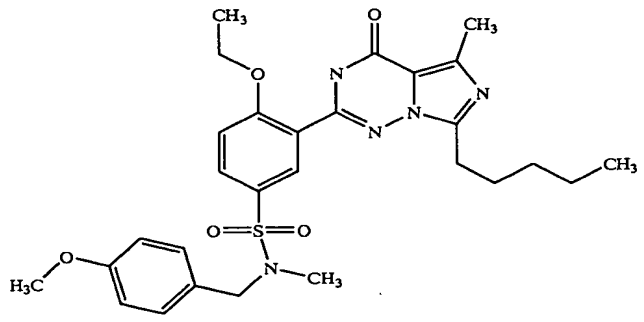
333		489.598	83	490
334		523.6592	89	524
335		594.7822	85	595
336		553.6857	85	554

TABLE 1-continued

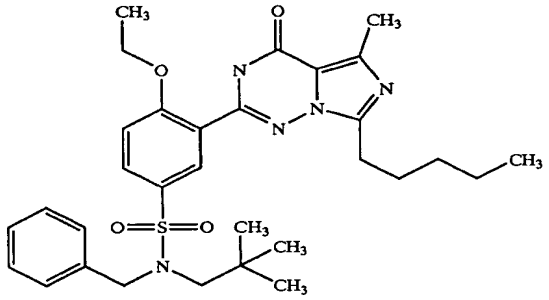
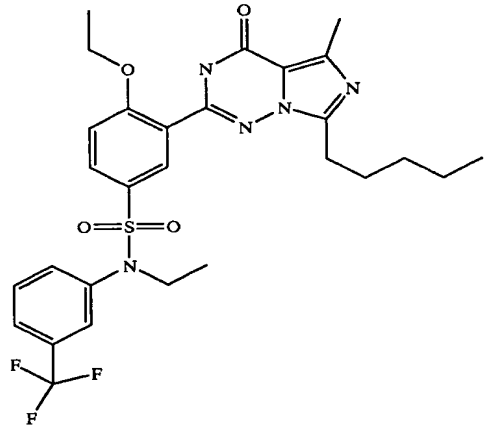
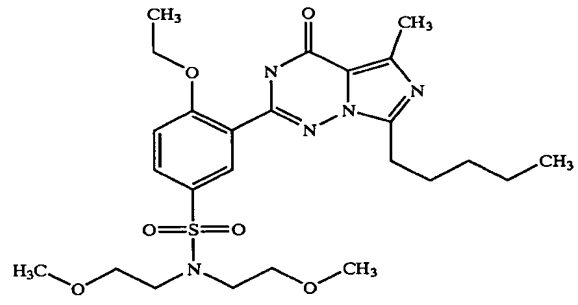
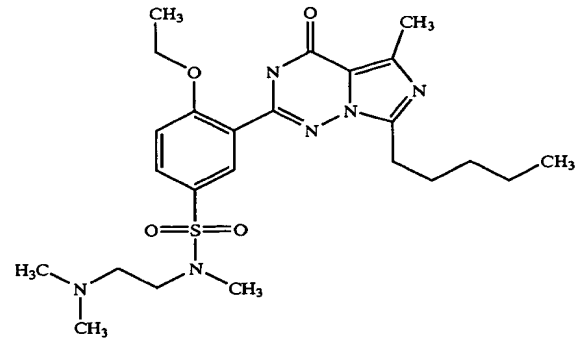
337		579.7675	80	580
338		591.6575	84	592
339		535.6675	89	536
340		504.6563	91	505

TABLE 1-continued

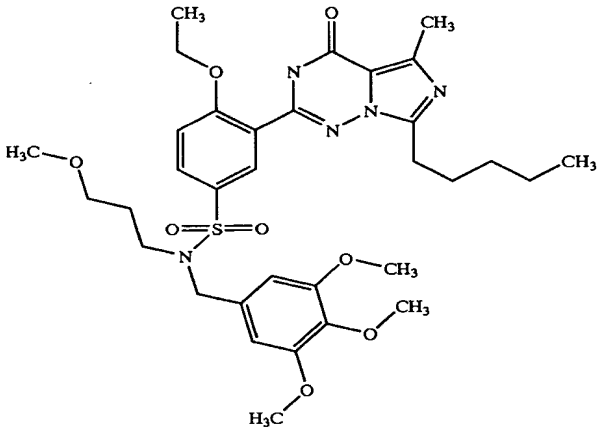
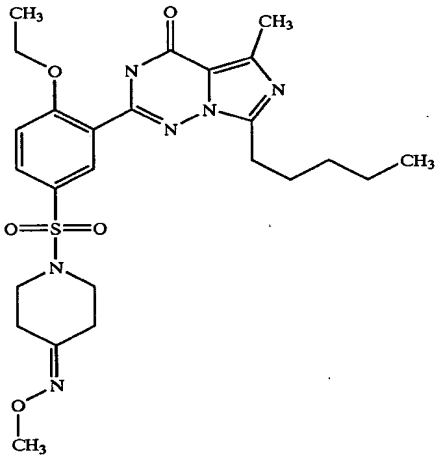
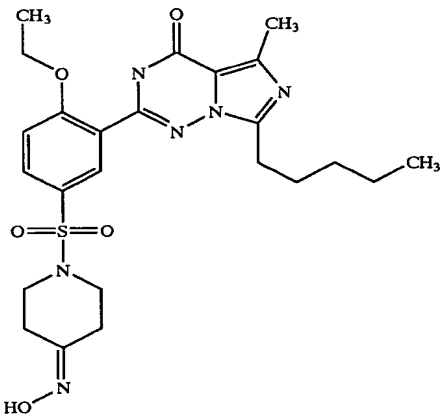
341		671.8193	79	672
342		530.6509	89	531
343		516.6238	85	517

TABLE 1-continued

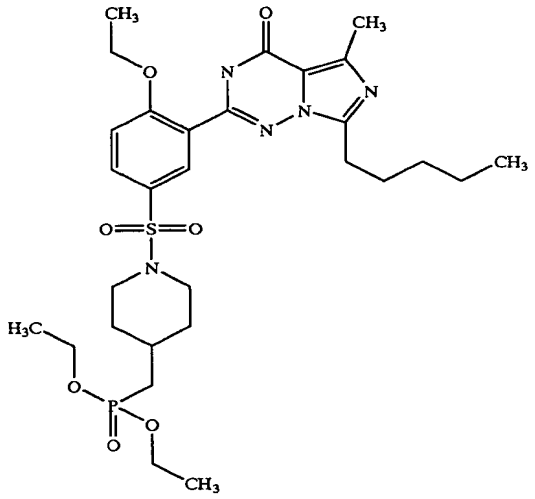
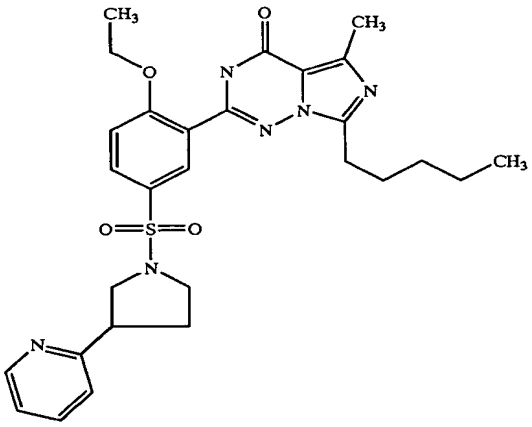
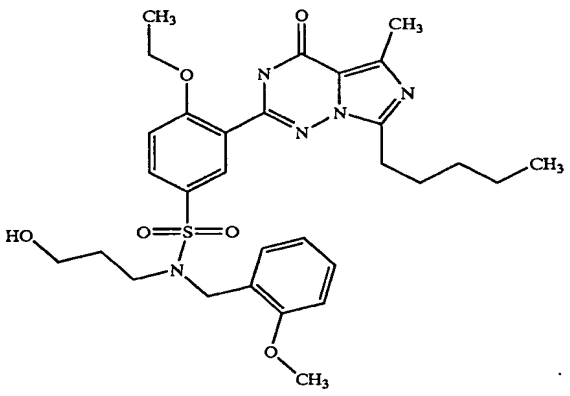
344		637.7411	78	638
345		550.685	86	551
346		597.7392	83	598

TABLE 1-continued

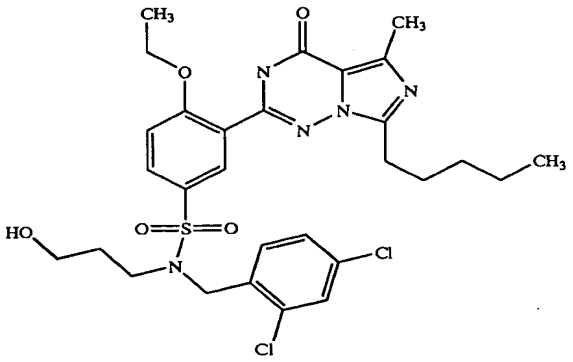
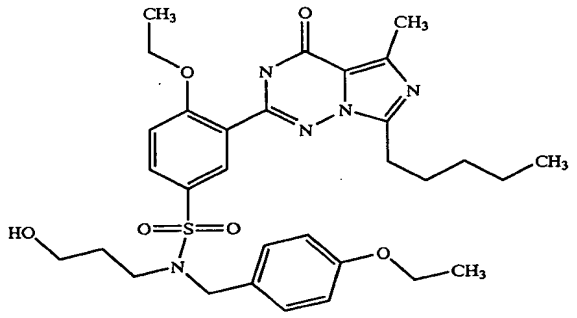
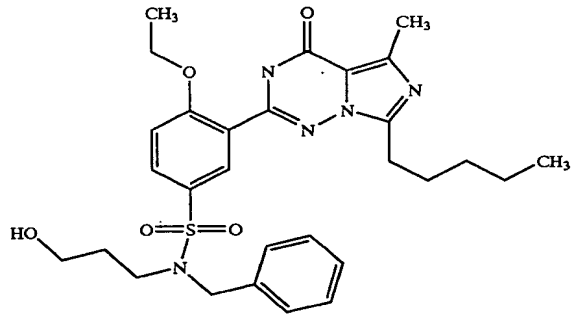
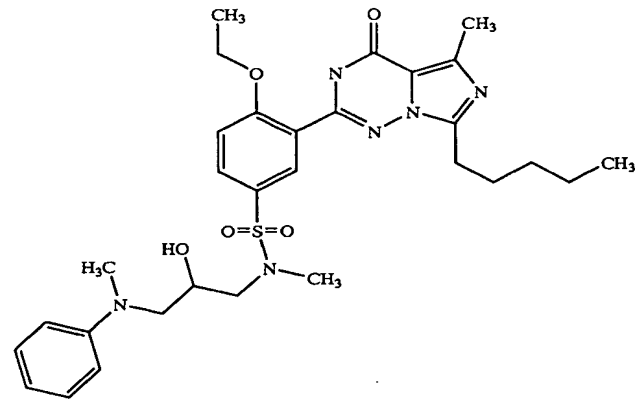
347		636.6028	82	636
348		611.7663	78	612
349		567.7127	80	568
350		596.7545	82	597

TABLE 1-continued

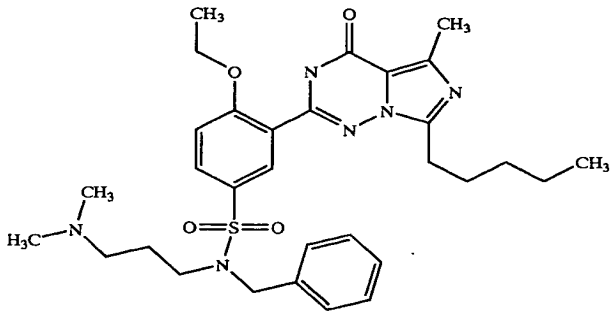
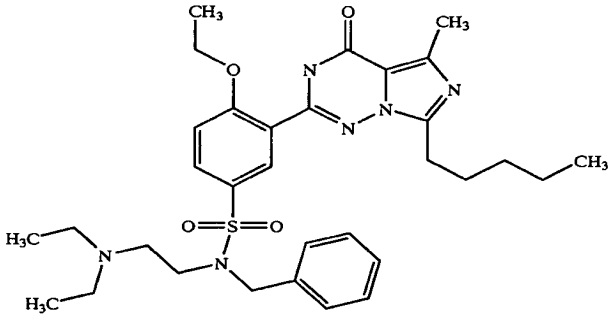
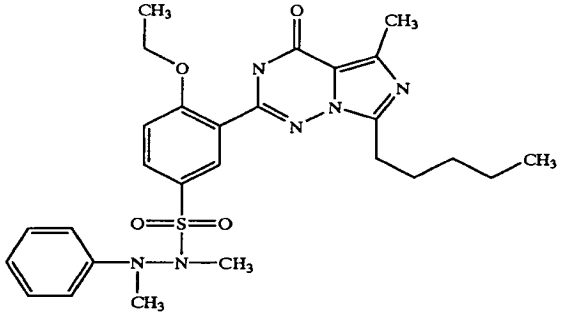
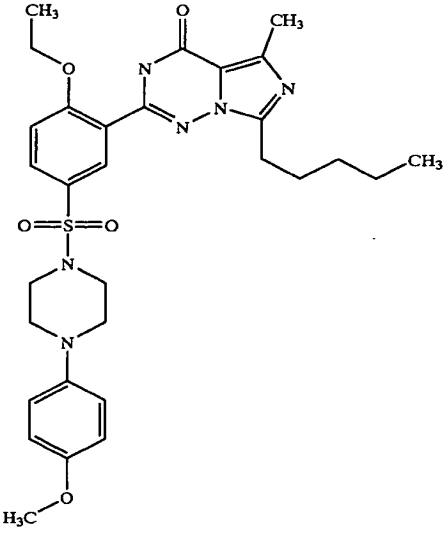
351		594.7822	79	595
352		608.8093	84	609
353		566.728	82	567
354		594.7386	85	595

TABLE 1-continued

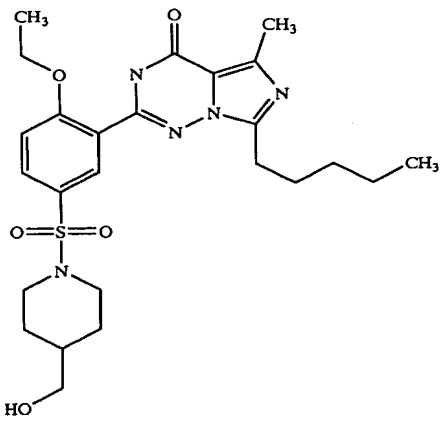
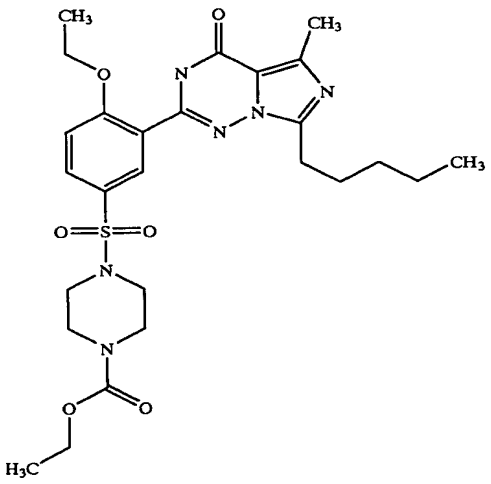
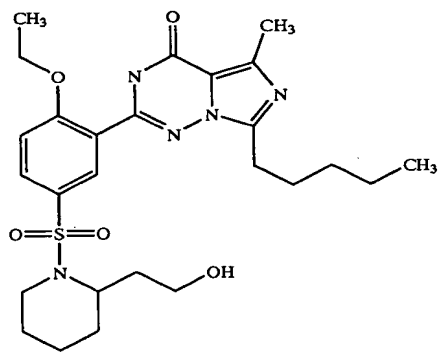
355		517.6522	85	518
356		560.6774	83	561
357		531.6793	84	532

TABLE 1-continued

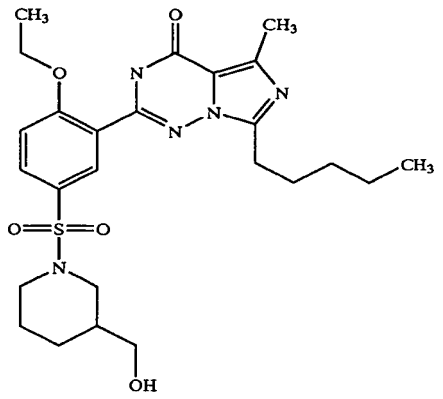
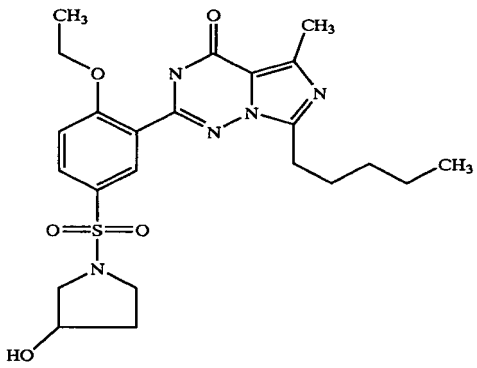
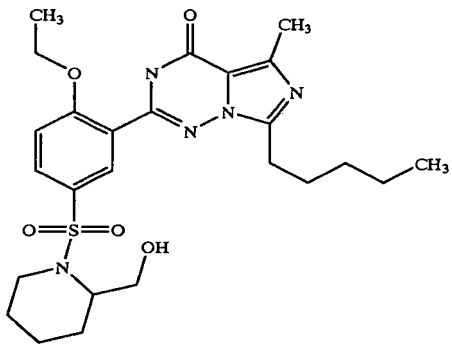
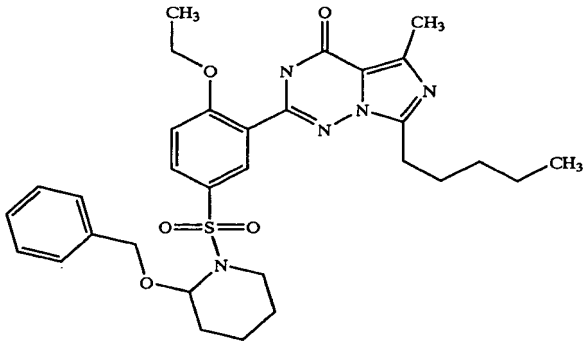
358		517.6522	85	518
359		489.598	85	490
360		517.6522	84	518
361		593.751	81	594

TABLE 1-continued

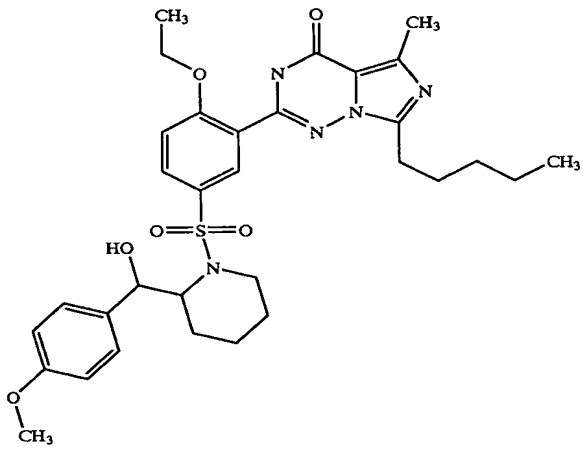
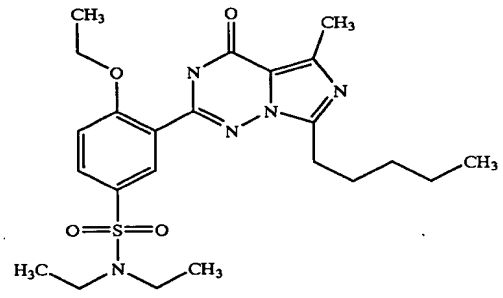
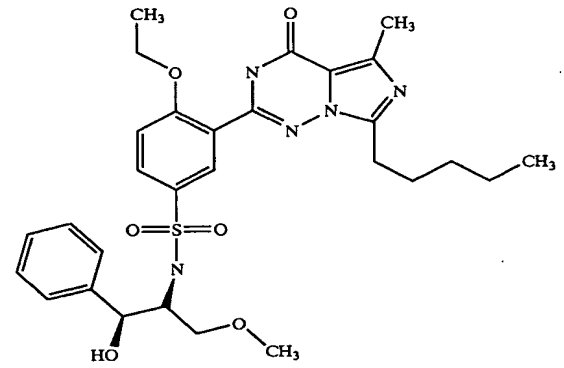
362		623.7775	50	624
363		475.6146	90	476
364		583.7121	76	584

TABLE 1-continued

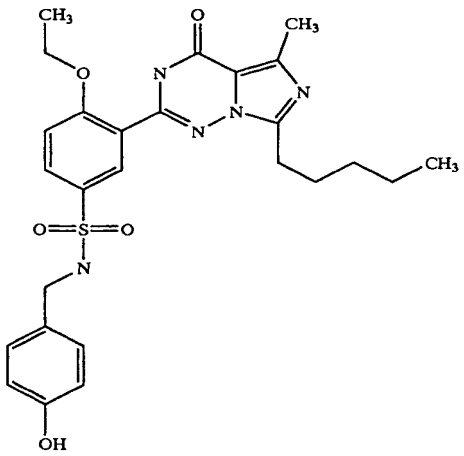
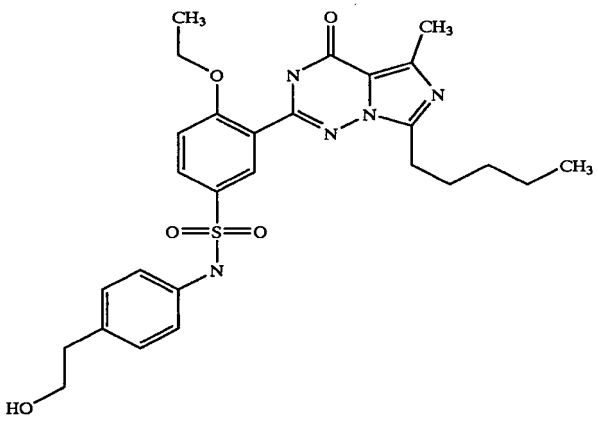
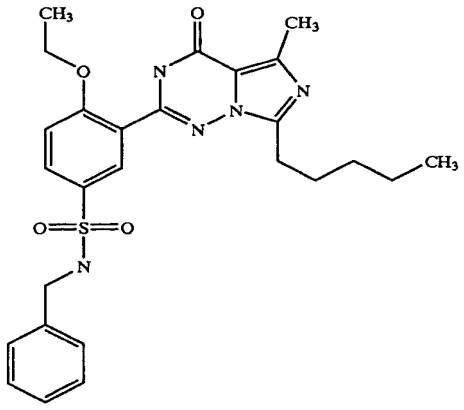
365		525.6315	69	526
366		539.6586	71	540
367		509.6321	56	510

TABLE 1-continued

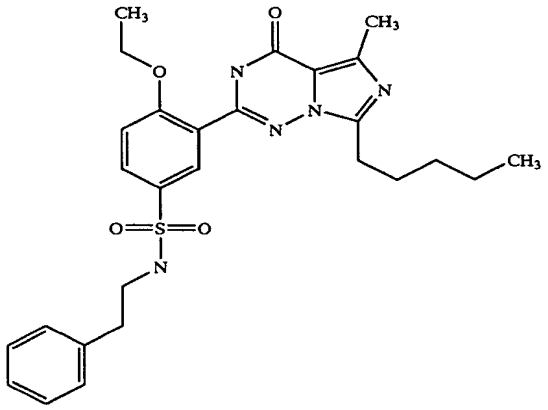
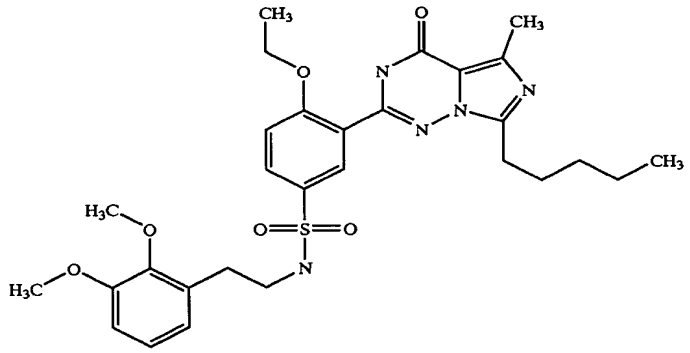
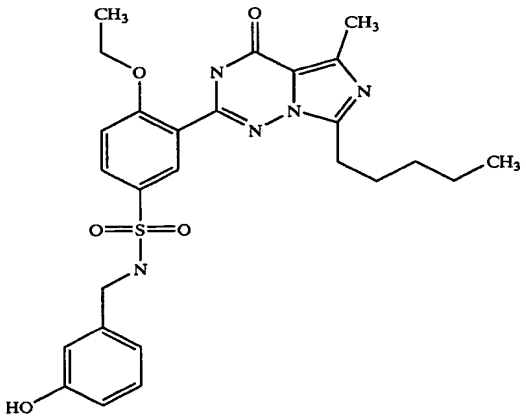
368		523.6592	86	524
369		583.7121	80	584
370		525.6315	72	526

TABLE 1-continued

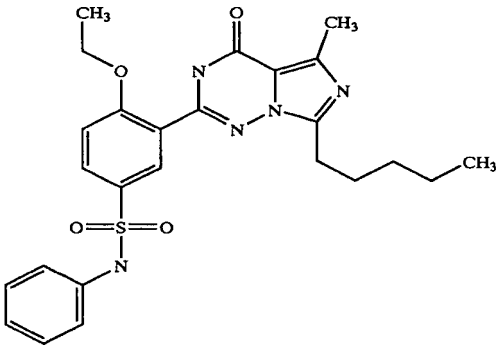
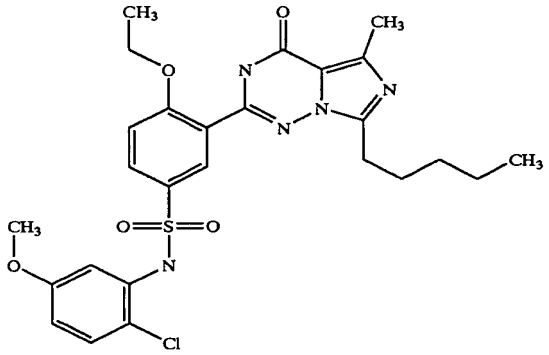
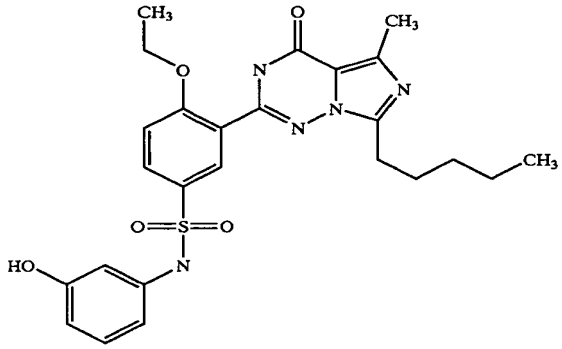
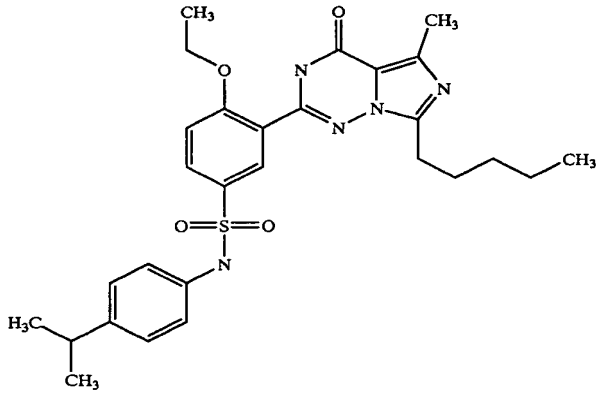
371		495.605	83	496
372		560.0765	52	560
373		511.6044	73	512
374		537.6863	81	538

TABLE 1-continued

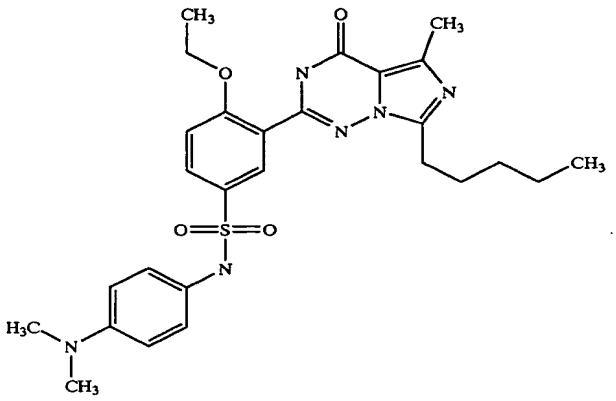
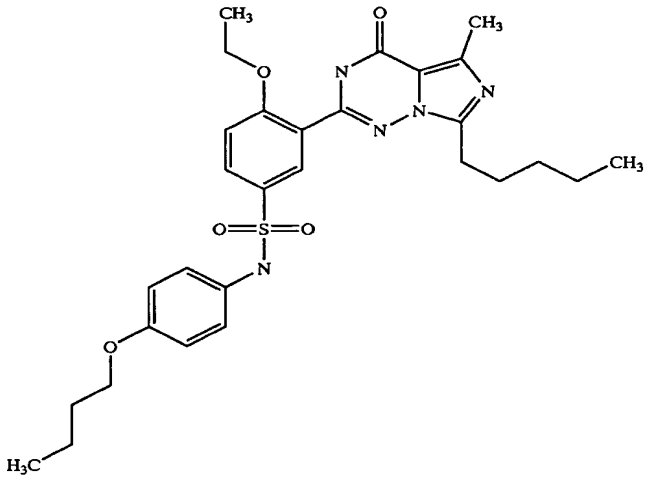
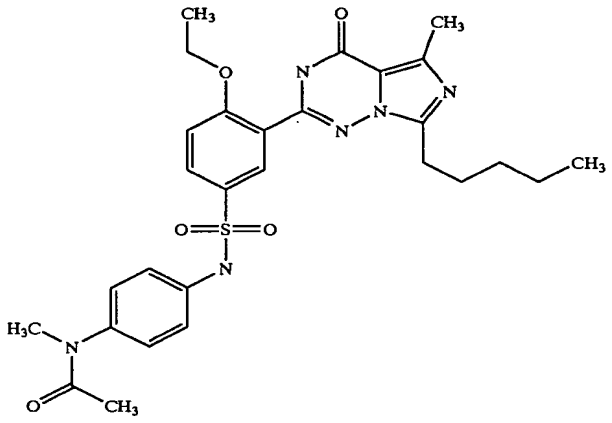
375		538.6738	74	539
376		567.7127	74	568
377		566.6844	88	567

TABLE 1-continued

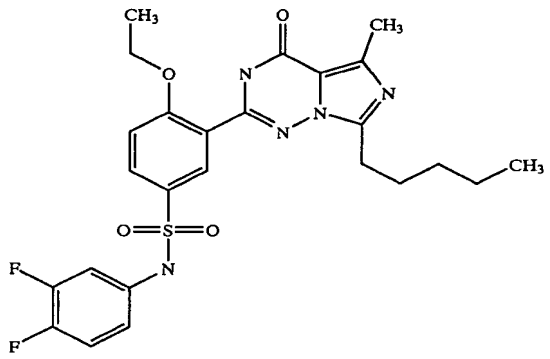
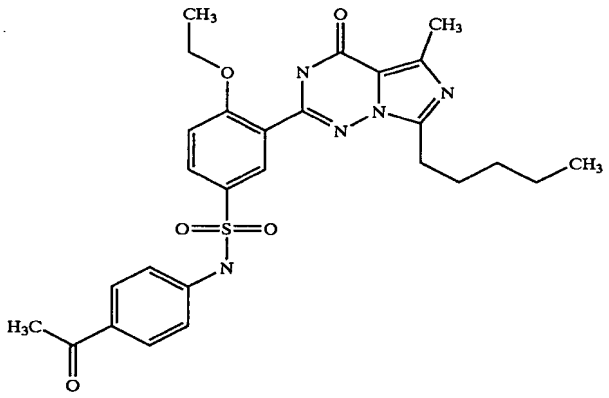
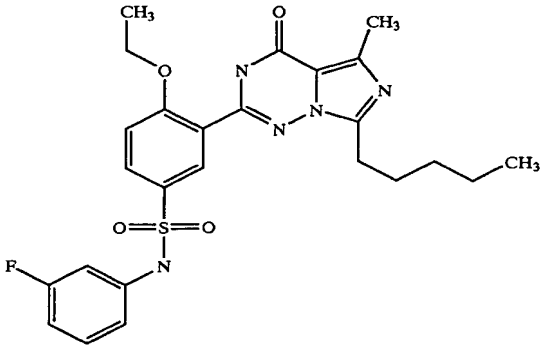
378		531.5858	82	532
379		537.6426	47	538
380		513.5954	83	514

TABLE 1-continued

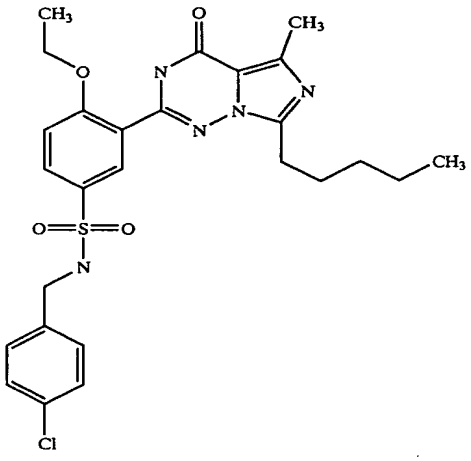
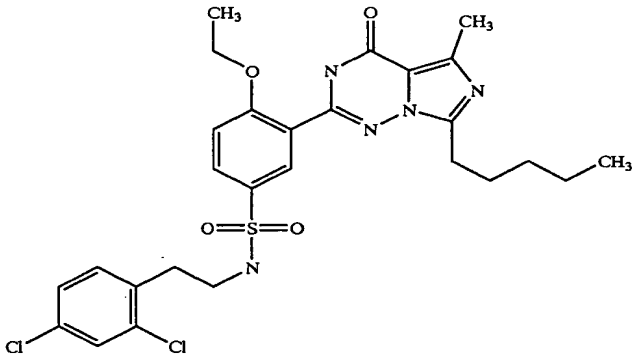
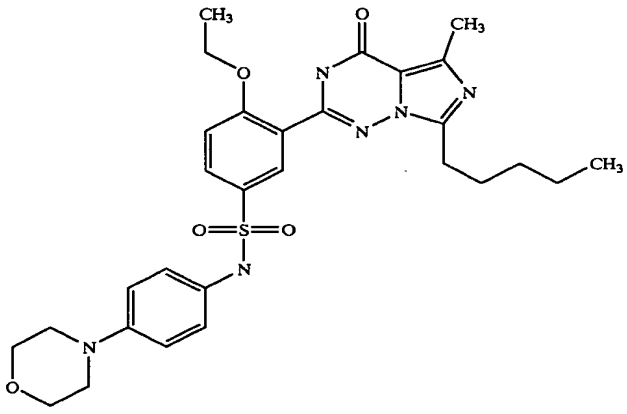
381		544.0771	82	545
382		592.5492	72	593
383		580.7115	70	581

TABLE 1-continued

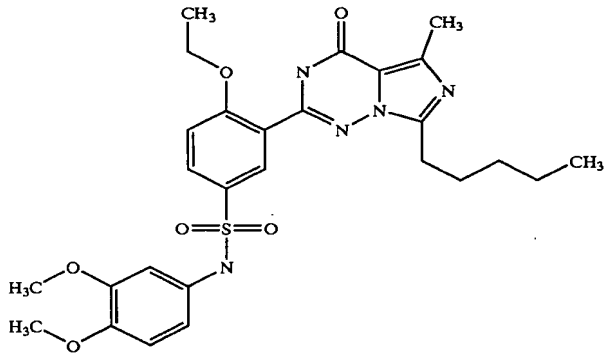
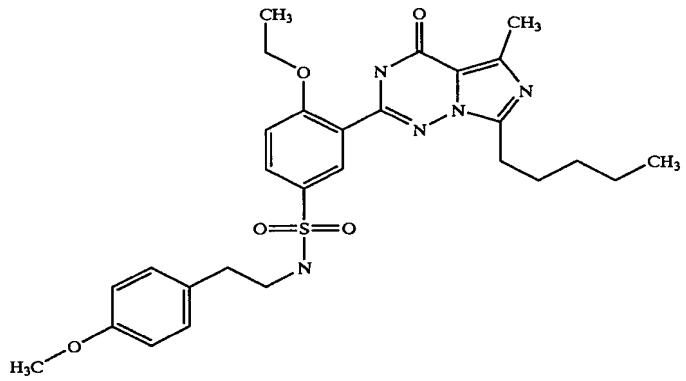
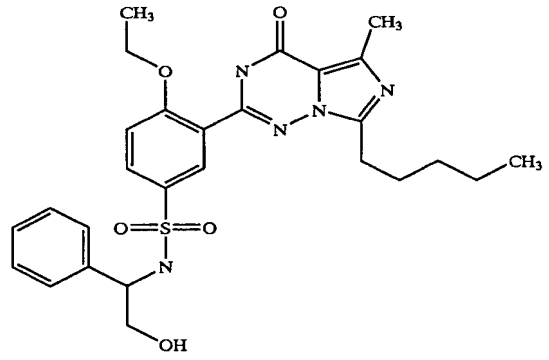
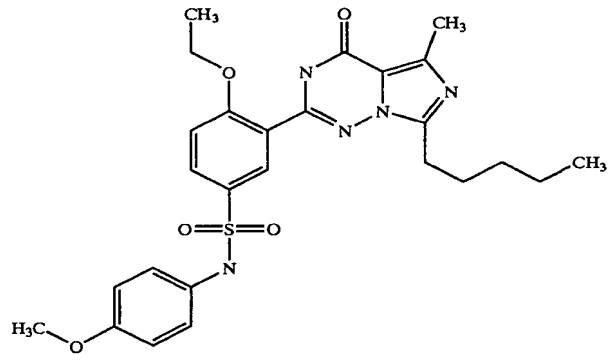
384		555.658	81	556
385		553.6857	80	554
386		539.6586	75	540
387		525.6315	86	526

TABLE 1-continued

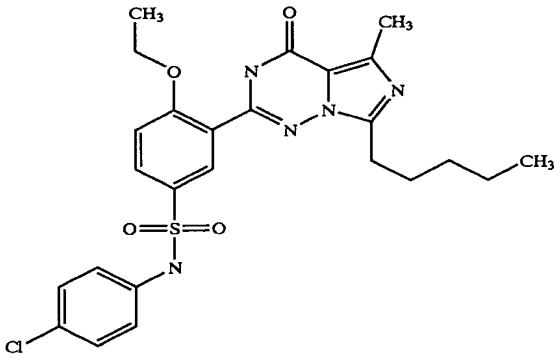
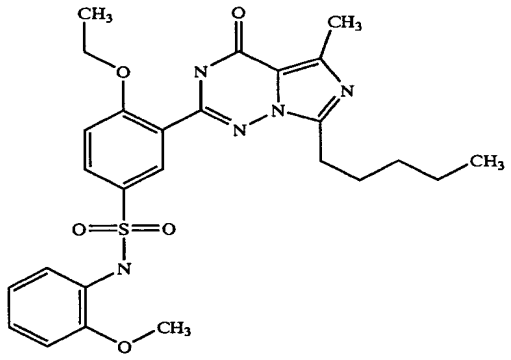
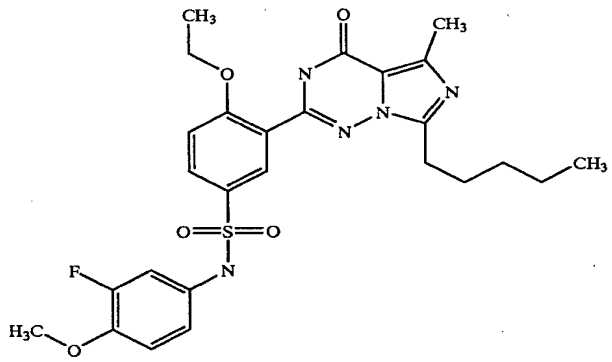
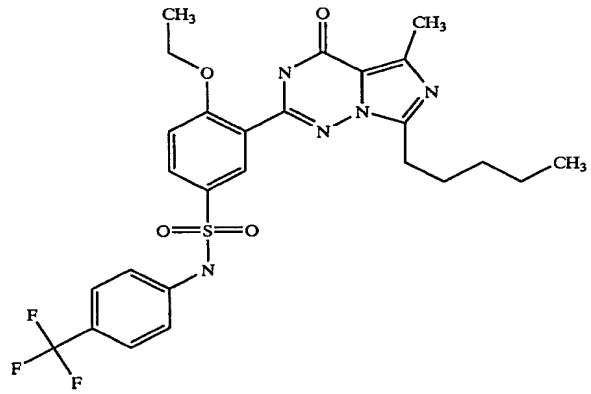
388		530.05	80	531
389		525.6315	86	526
390		543.6219	76	544
391		563.6034	81	564

TABLE 1-continued

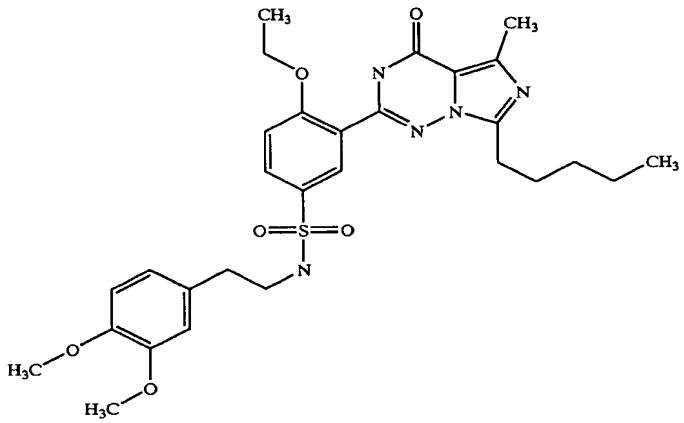
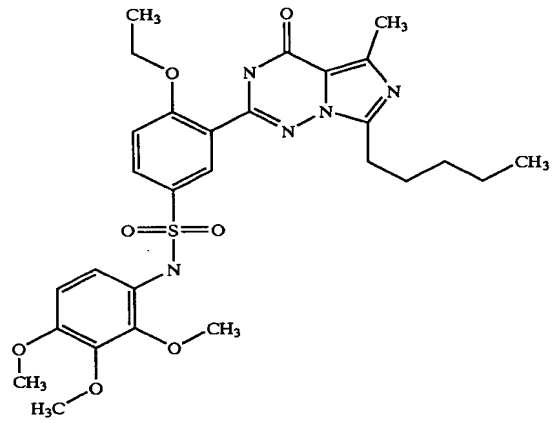
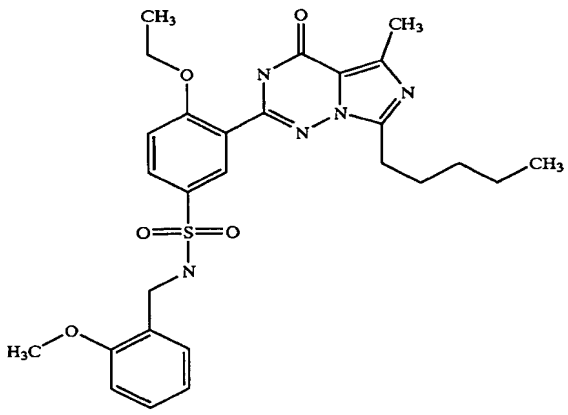
392		583.7121	79	584
393		585.6845	84	586
394		539.6586	80	540

TABLE 1-continued

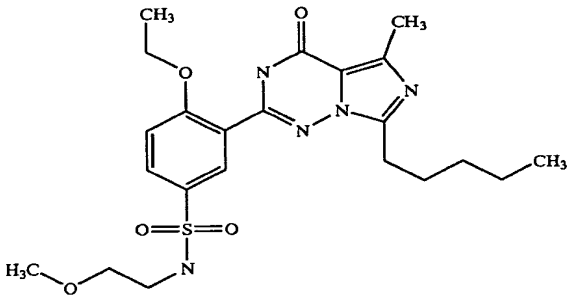
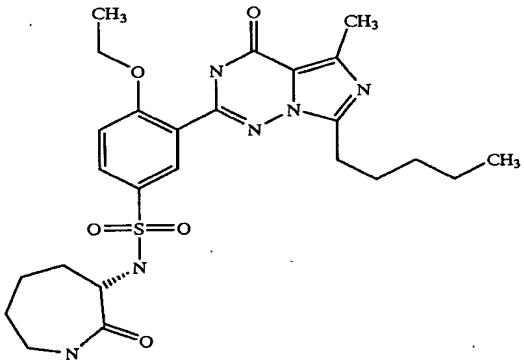
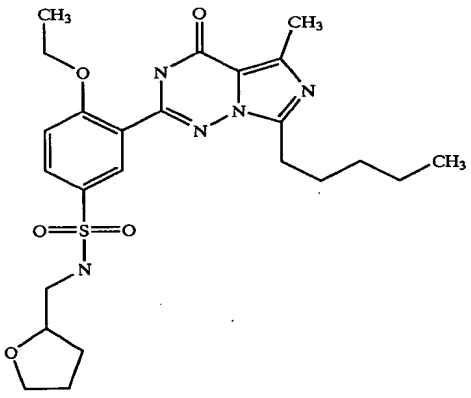
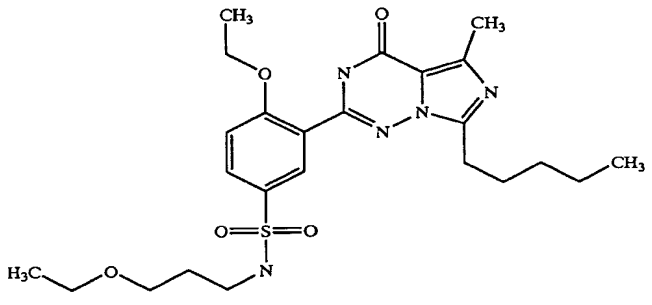
395		477.5869	87	478
396		530.6509	91	531
397		503.6251	87	504
398		505.6411	90	506

TABLE 1-continued

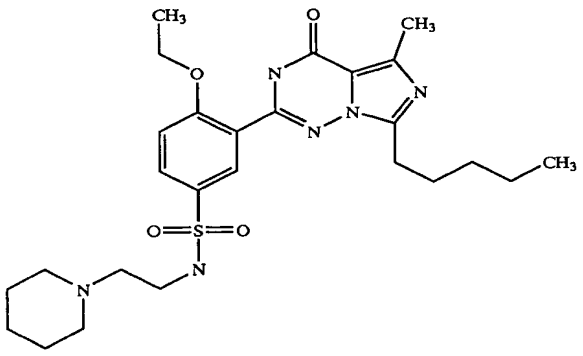
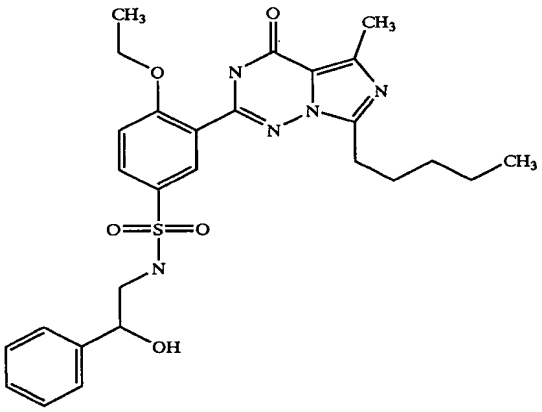
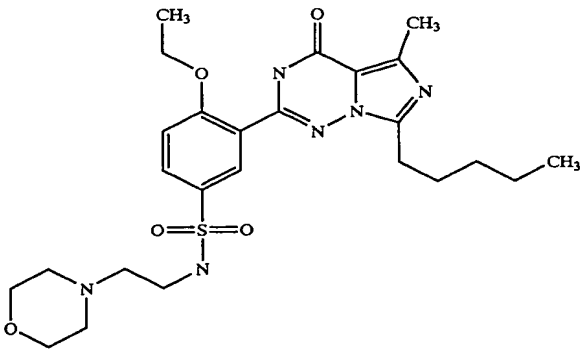
399		530.6946	51	531
400		539.6586	74	540
401		532.6669	70	533

TABLE 1-continued

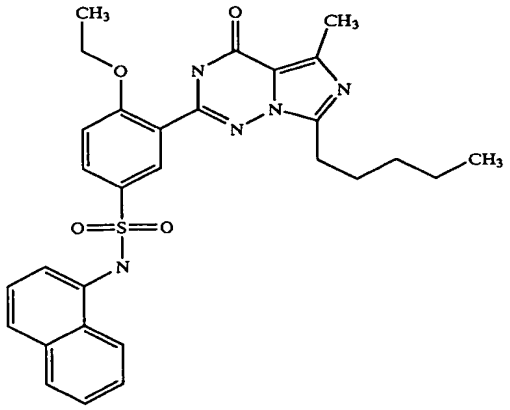
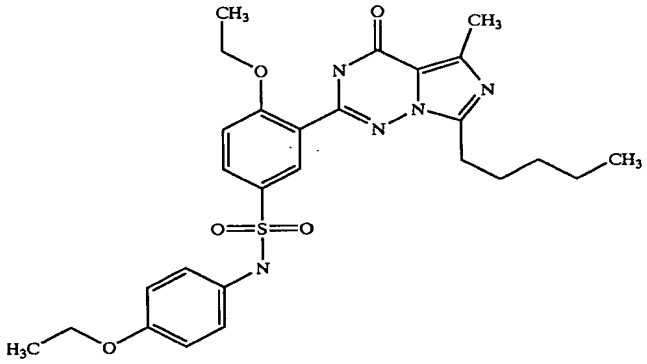
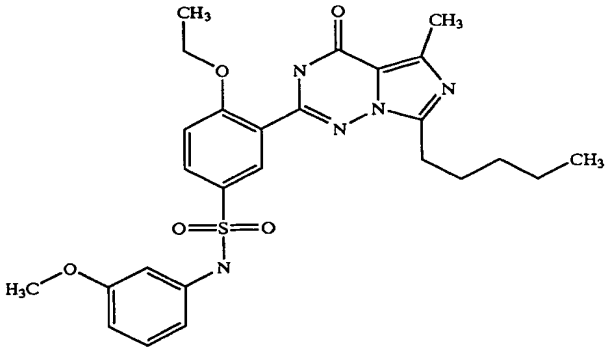
402		545.6655	79	546
403		539.6586	85	540
404		525.6315	81	526

TABLE 1-continued

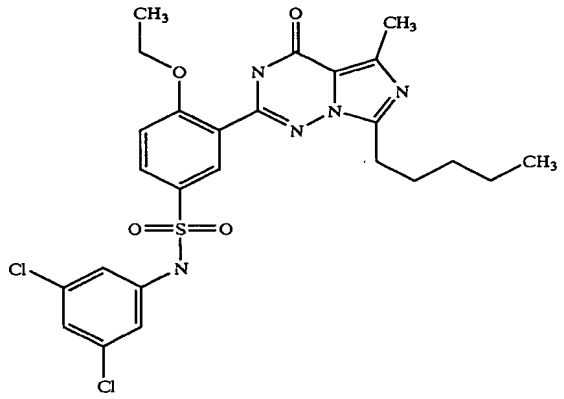
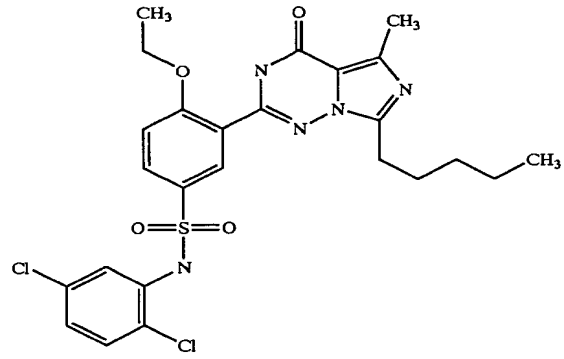
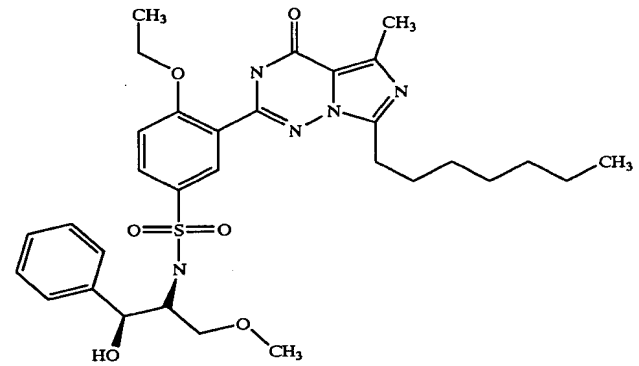
405		564.495	90	565
406		564.495	60	565
407		611.7663	84	612

TABLE 1-continued

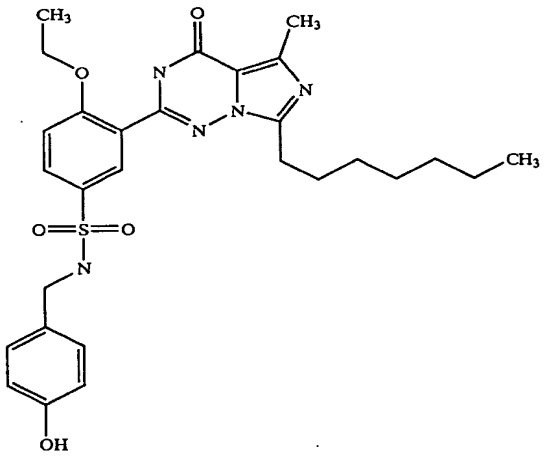
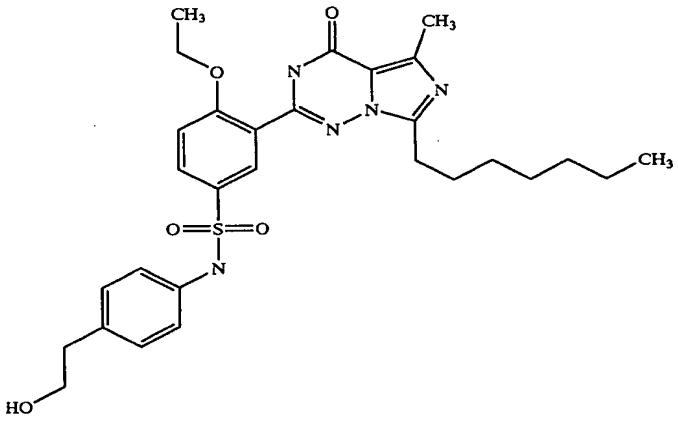
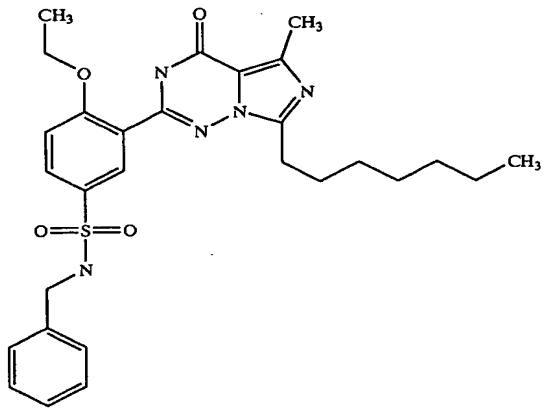
408		553.6857	79	554
409		567.7127	75	568
410		537.6863	80	538

TABLE 1-continued

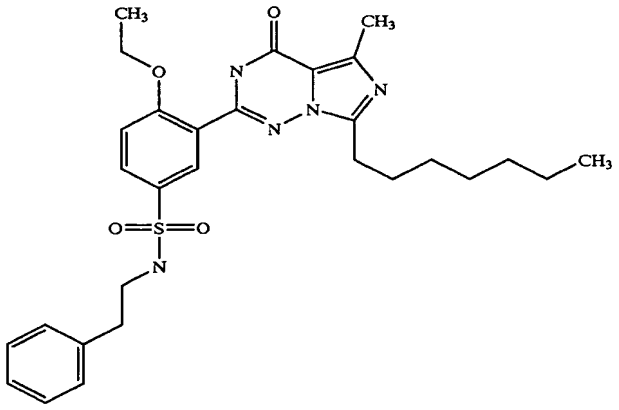
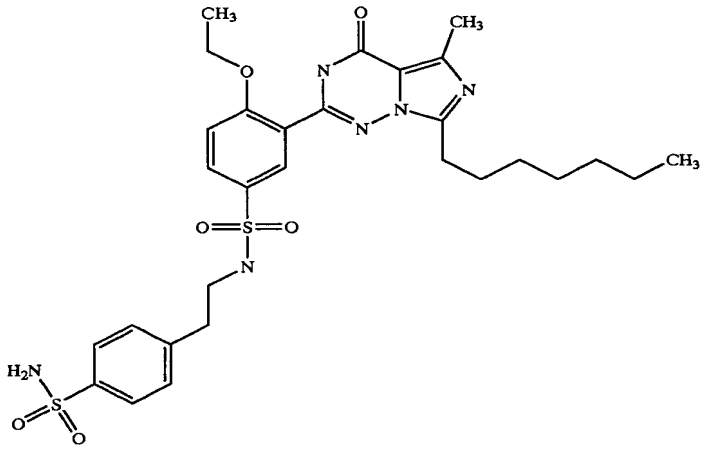
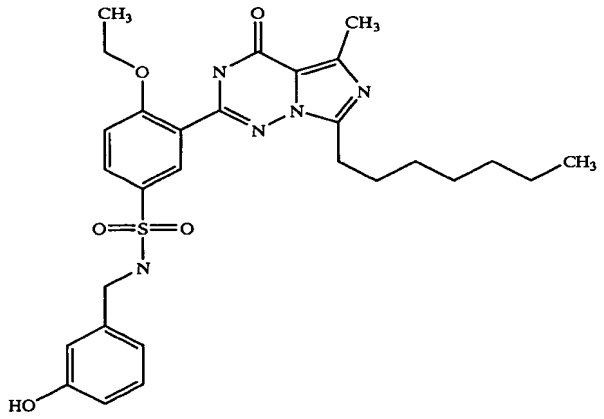
411		551.7133	86	552
412		630.7908	37	631
413		553.6857	66	554

TABLE 1-continued

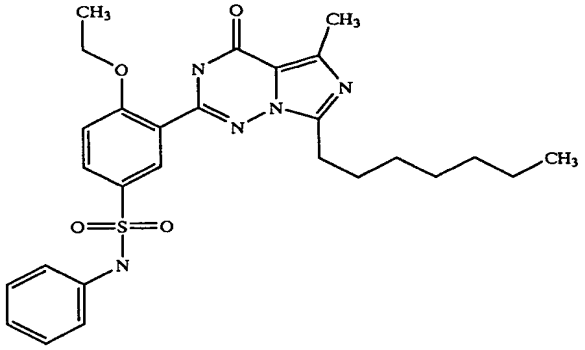
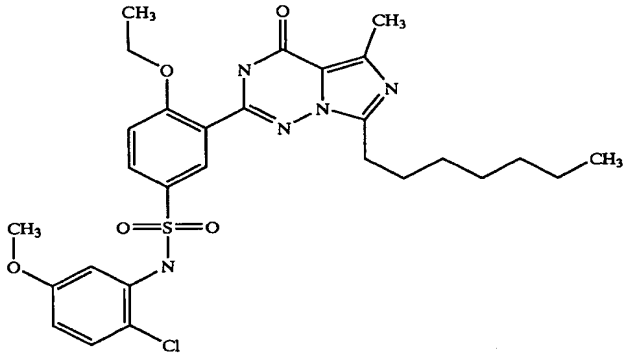
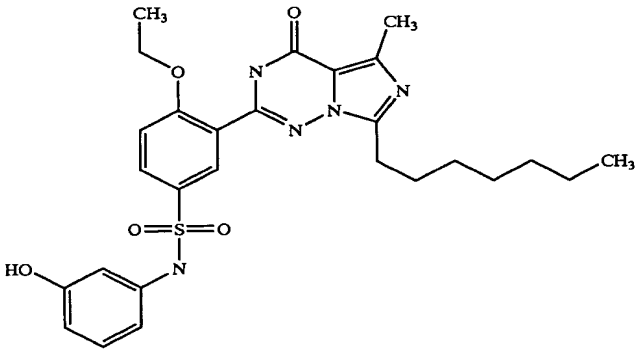
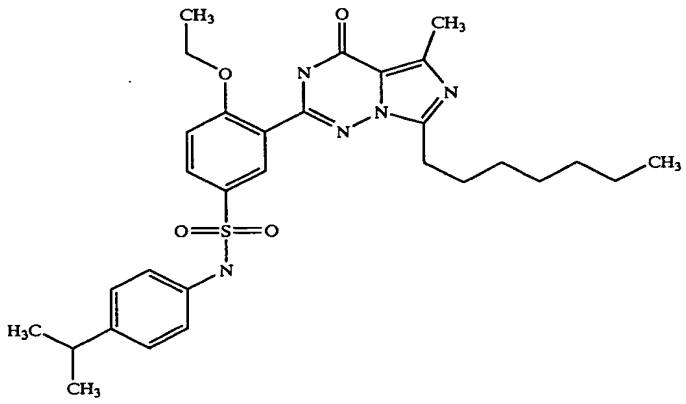
414		523.6592	82	524
415		588.1307	31	588
416		539.6586	77	540
417		565.7404	80	566

TABLE 1-continued

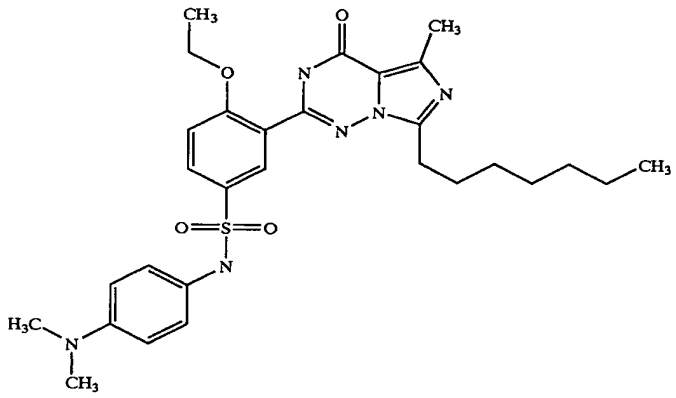
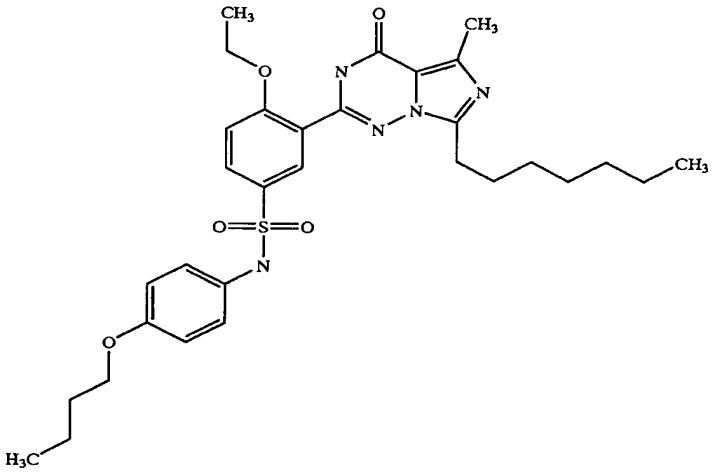
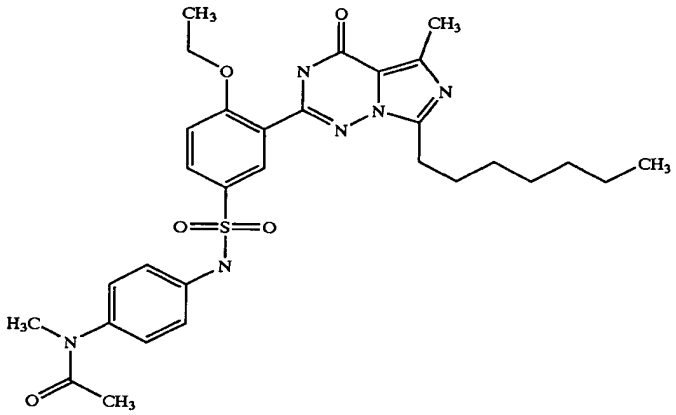
418		566.728	68	567
419		595.7669	84	596
420		594.7386	77	595

TABLE 1-continued

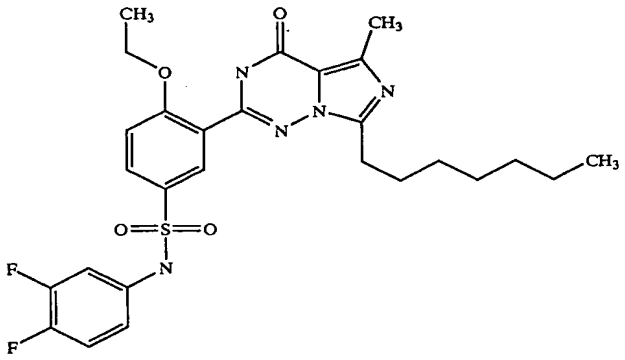
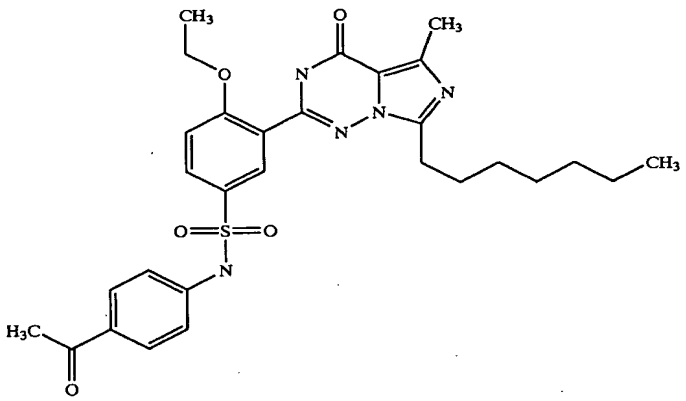
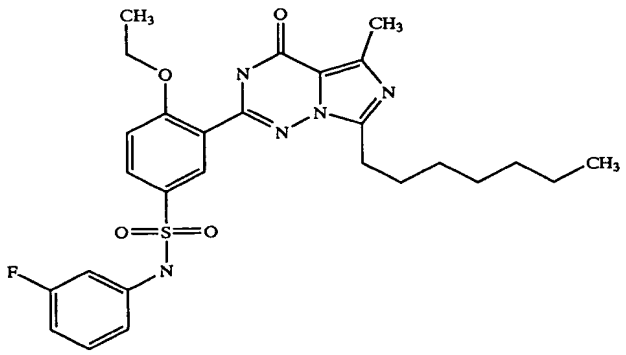
421		559.64	81	560
422		565.6968	42	566
423		541.6496	82	542

TABLE 1-continued

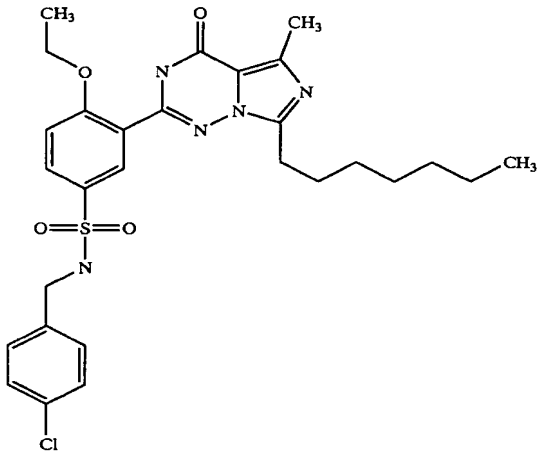
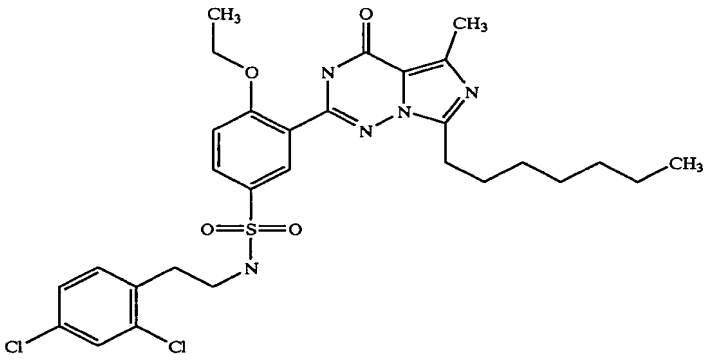
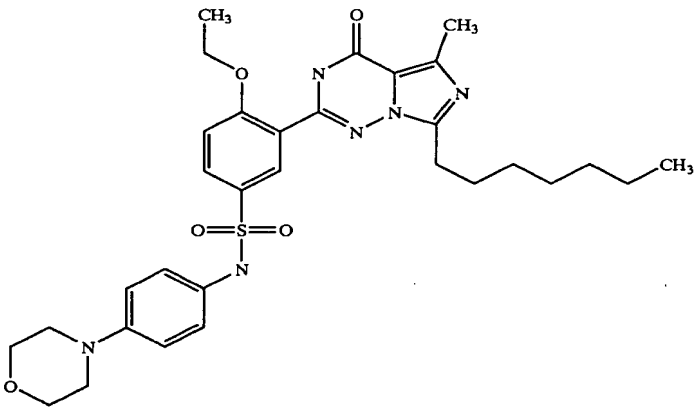
424		572.1313	85	572
425		620.6034	80	620
426		608.7657	84	609

TABLE 1-continued

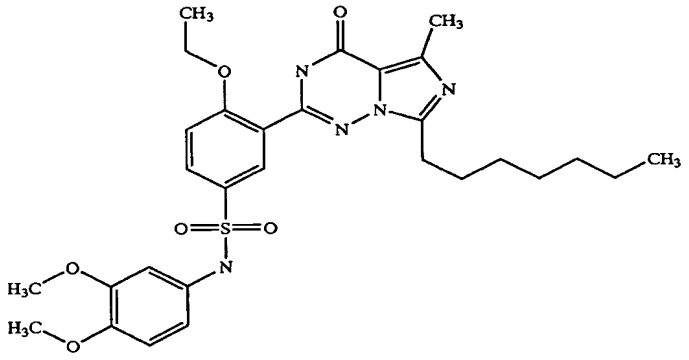
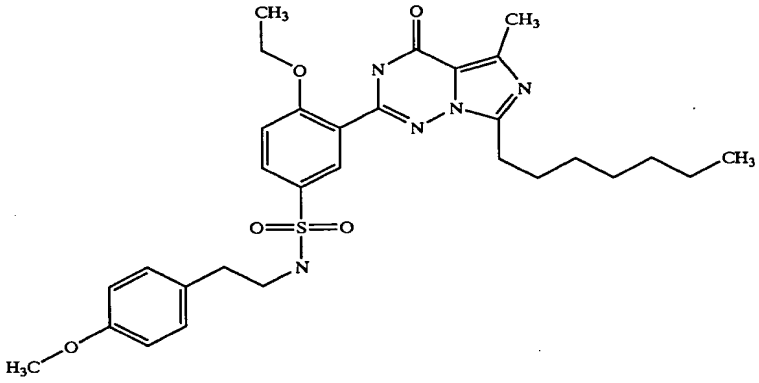
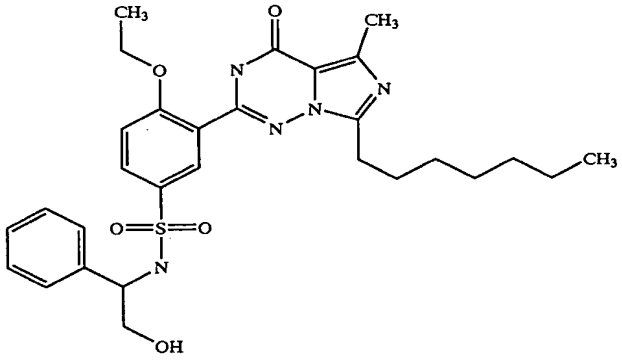
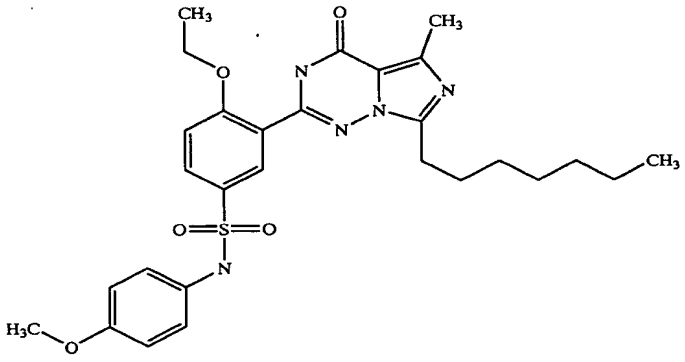
427		583.7121	82	584
428		581.7398	77	582
429		567.7127	80	568
430		553.6857	82	554

TABLE 1-continued

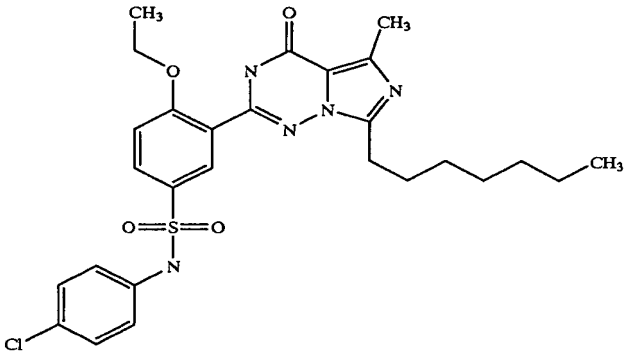
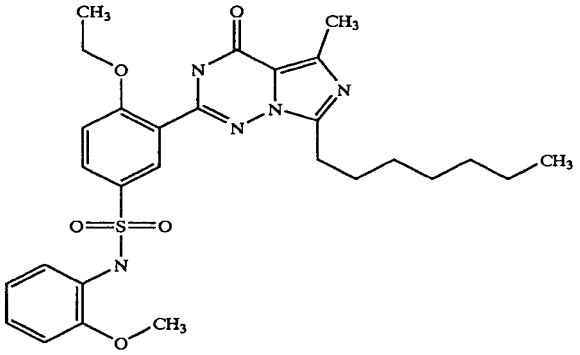
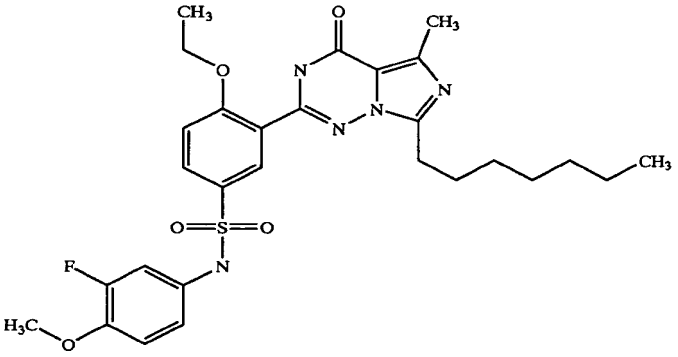
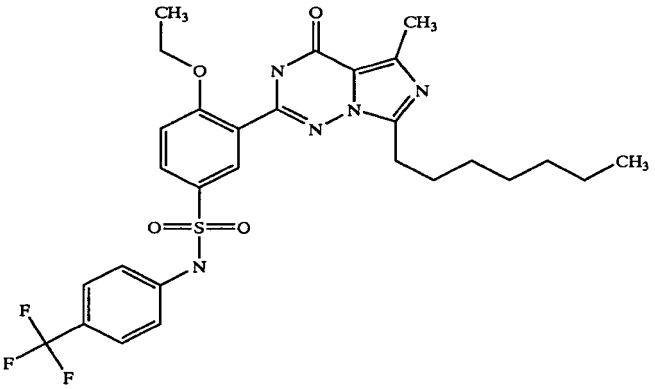
431		558.1042	80	558
432		553.6857	85	554
433		571.6761	79	572
434		591.6575	83	592

TABLE 1-continued

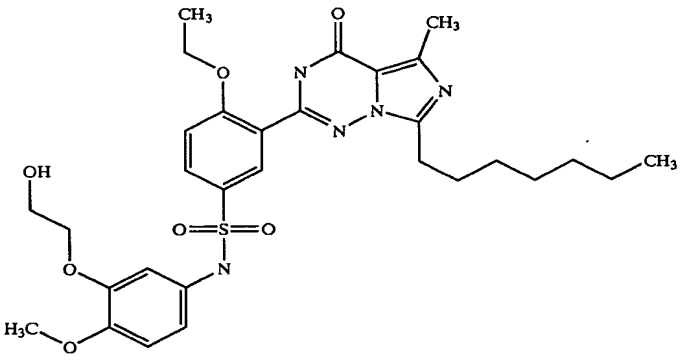
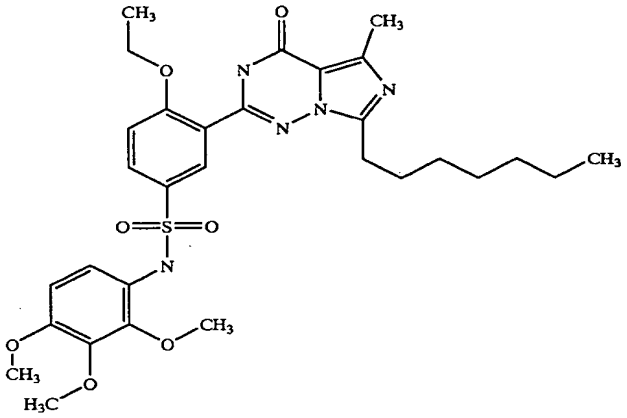
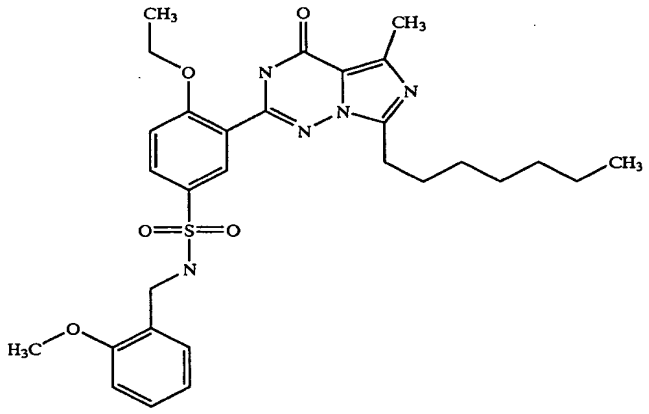
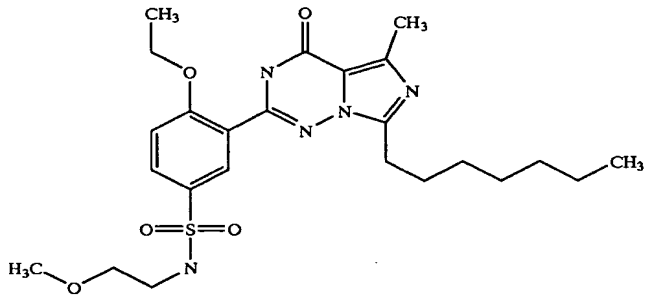
435		613.7386	77	614
436		613.7386	82	614
437		567.7127	84	568
438		505.6411	85	506

TABLE 1-continued

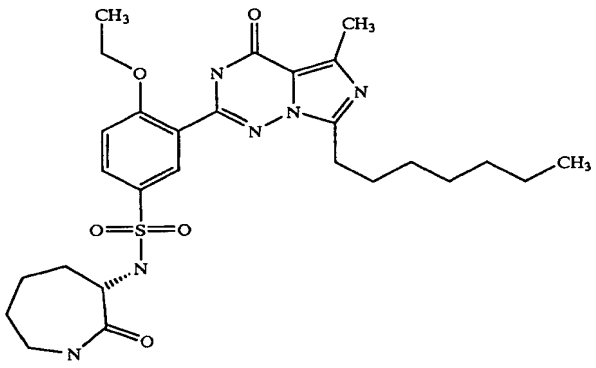
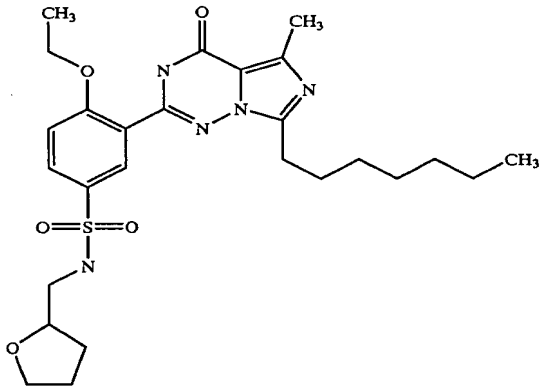
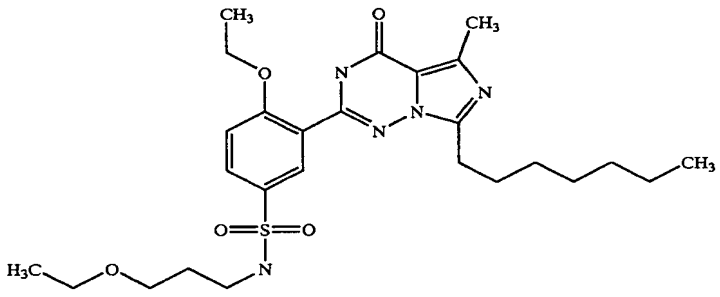
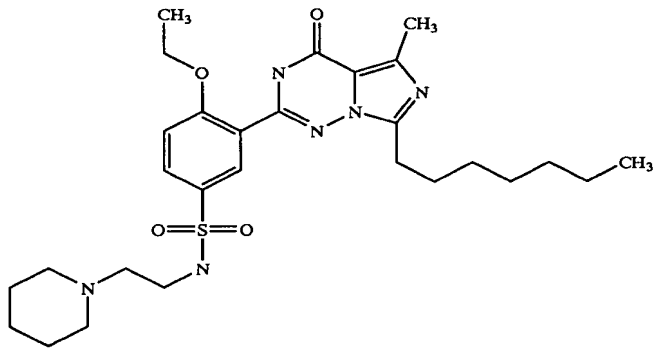
439		558.7051	90	559
440		531.6793	87	532
441		533.6952	90	534
442		558.7487	75	559

TABLE 1-continued

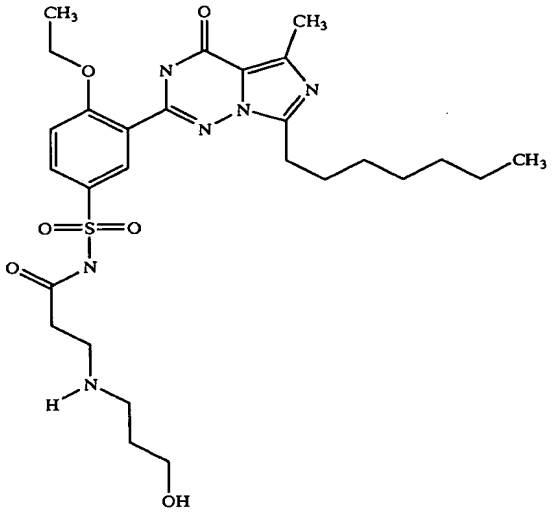
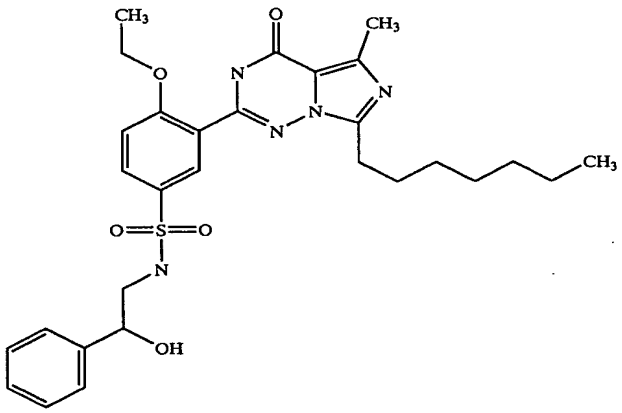
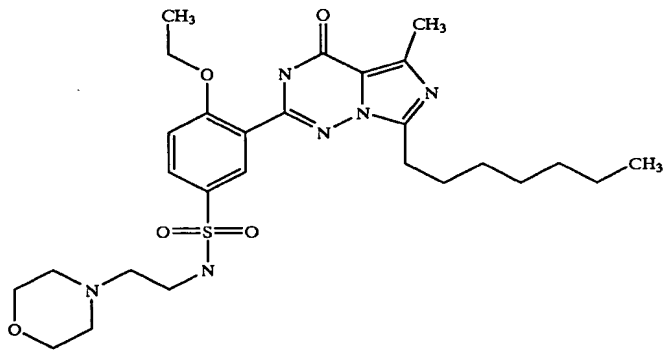
443		576.7205	66	577
444		567.7127	77	568
445		560.7211	79	561

TABLE 1-continued

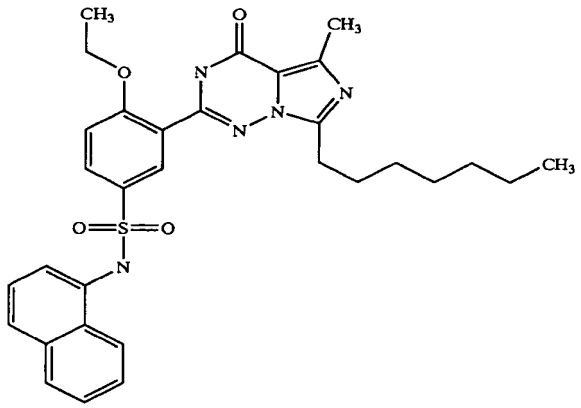
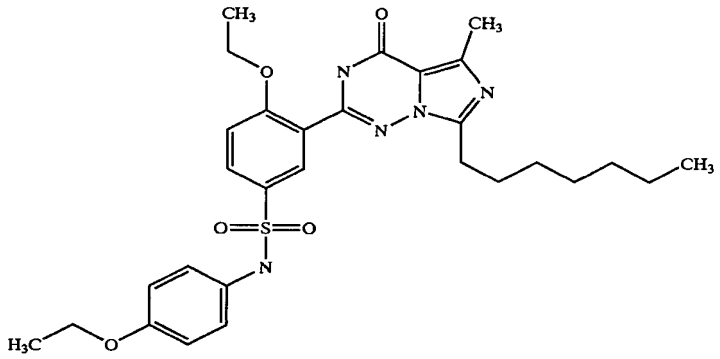
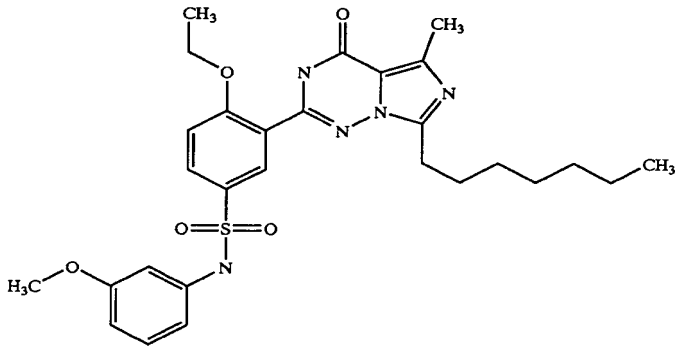
446		573.7197	76	574
447		567.7127	80	568
448		553.6857	83	554

TABLE 1-continued

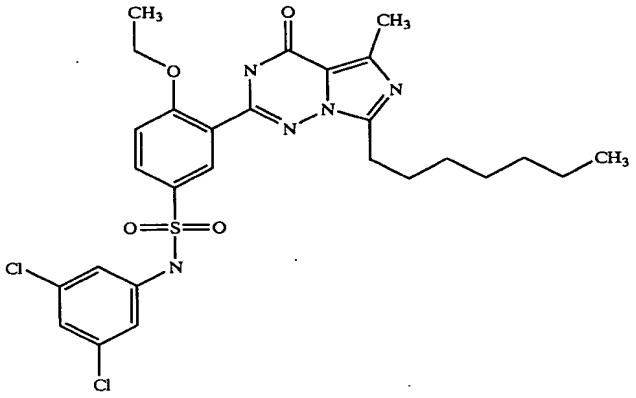
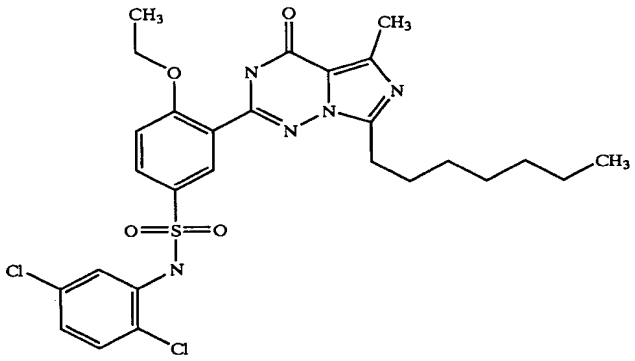
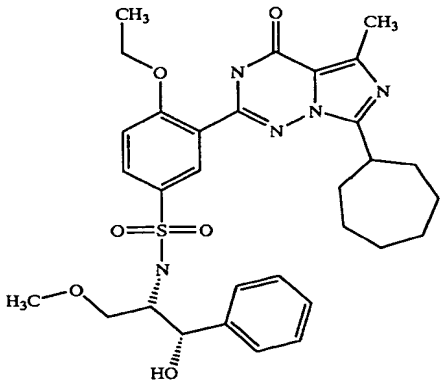
449		592.5492	30	592
450		592.5492	43	592
451		609.750	78	610

TABLE 1-continued

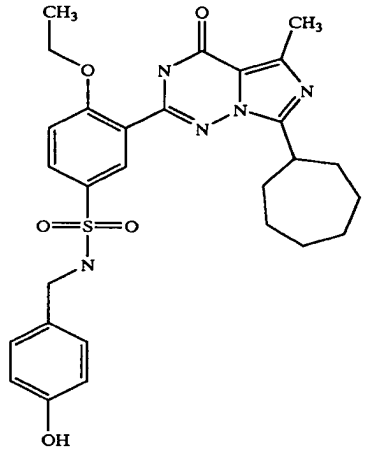
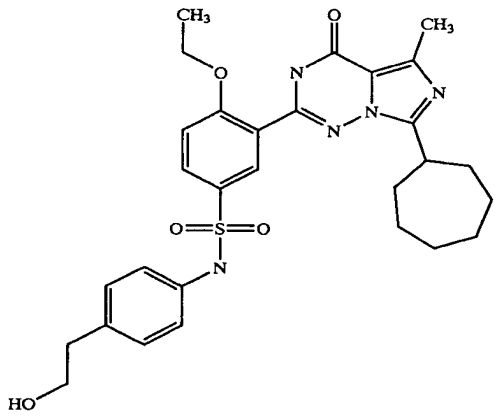
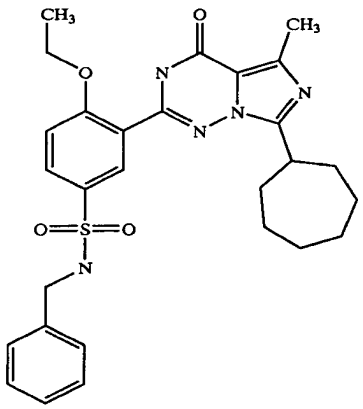
452		551.670	74	552
453		565.697	65	566
454		535.670	80	536

TABLE 1-continued

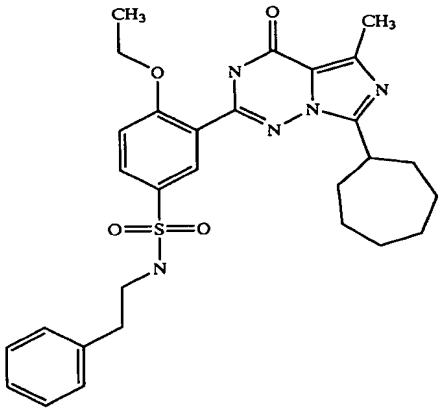
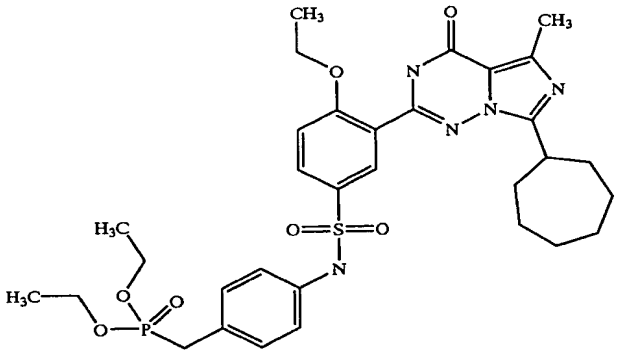
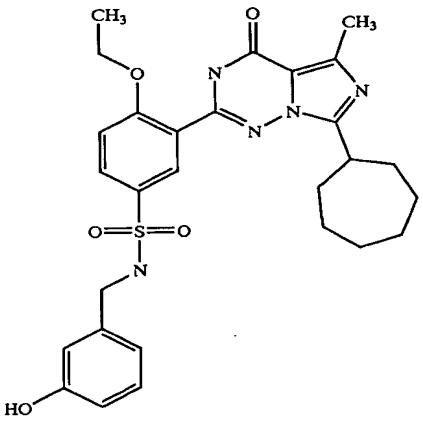
455		549.697	79	550
456		671.759	83	672
457		551.670	69	552

TABLE 1-continued

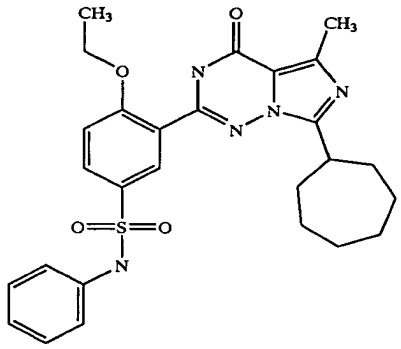
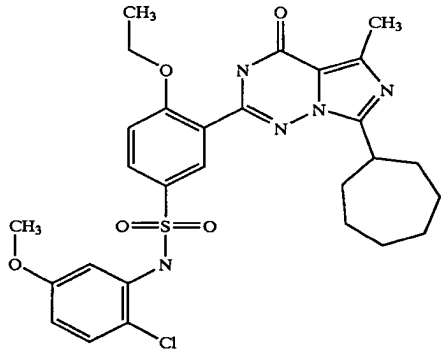
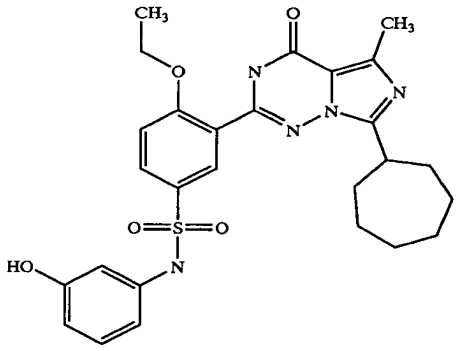
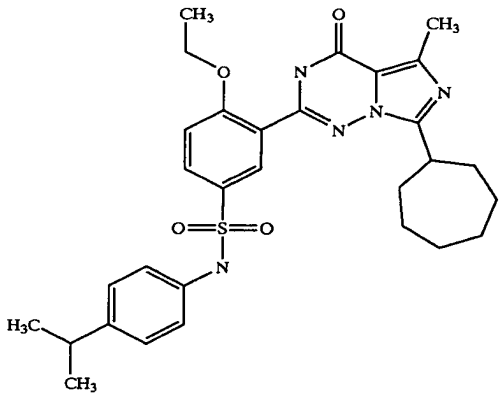
458		521.643	80	522
459		586.115	34	586
460		537.643	76	538
461		563.724	67	564

TABLE 1-continued

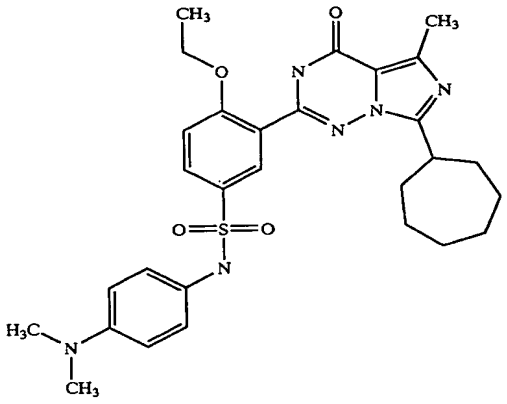
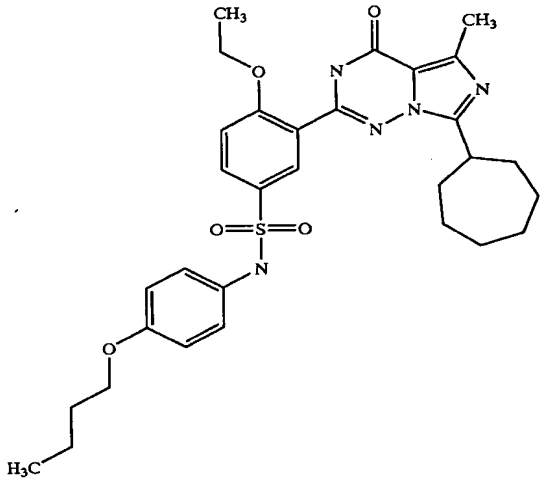
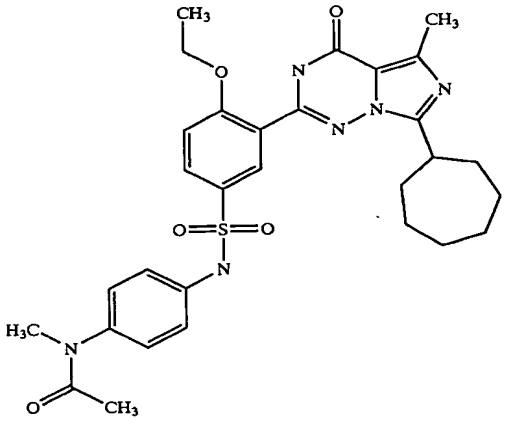
462		564.712	73	565
463		593.751	79	594
464		592.723	72	593

TABLE 1-continued

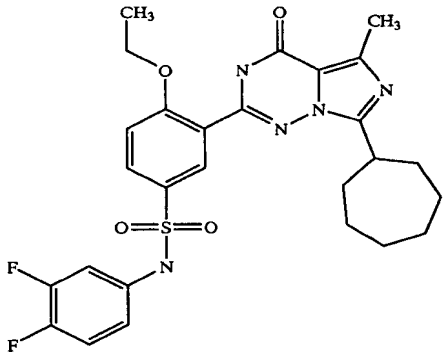
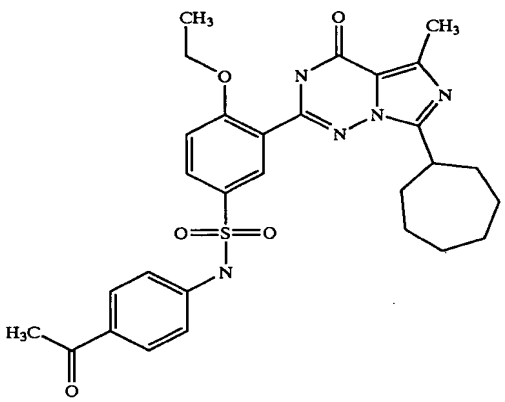
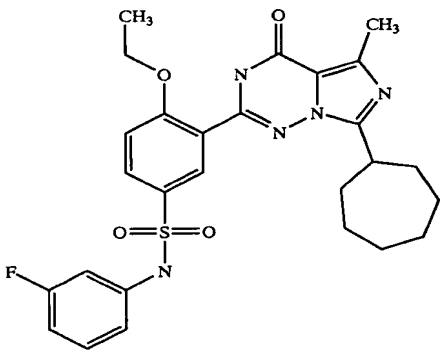
465		557.624	78	558
466		563.681	44	564
467		539.634	67	540

TABLE 1-continued

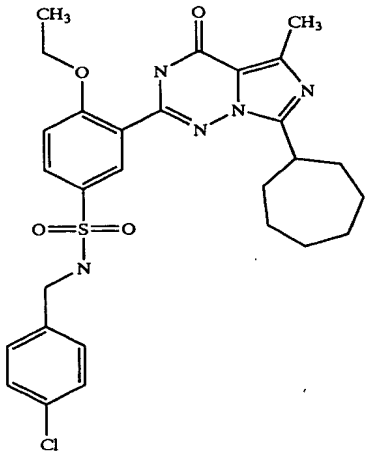
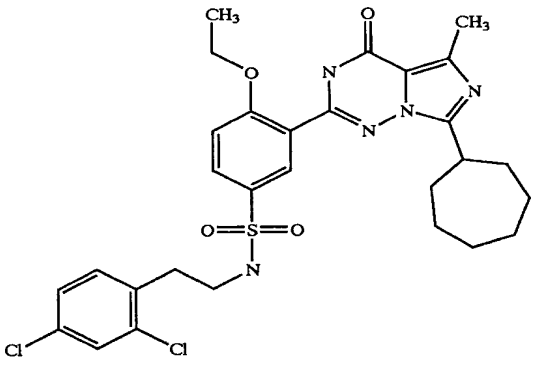
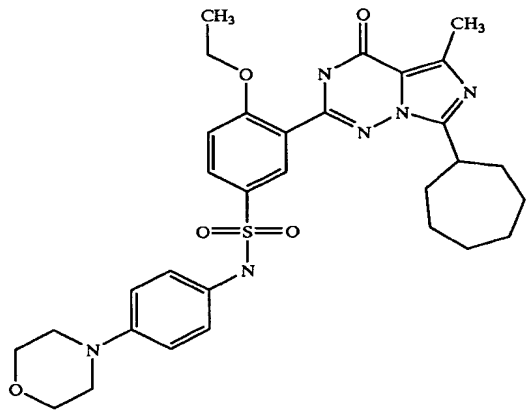
468		570.115	75	570
469		618.587	65	618
470		606.750	69	607

TABLE 1-continued

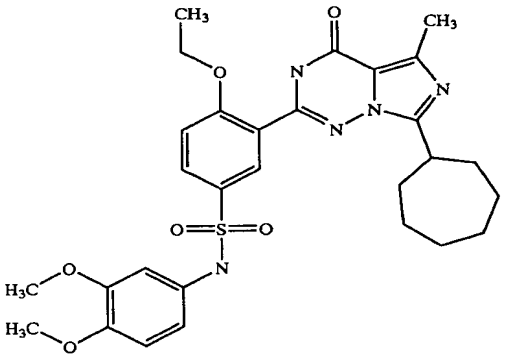
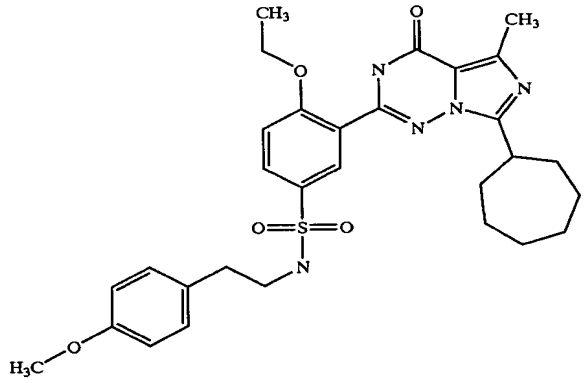
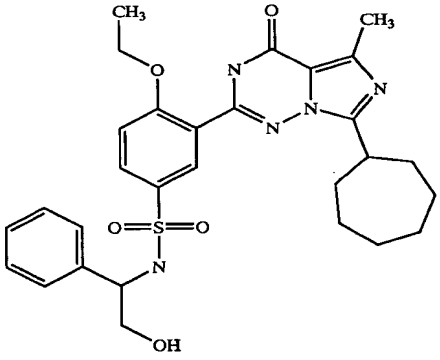
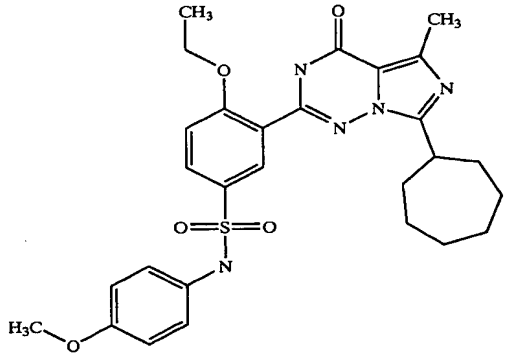
471		581.696	80	582
472		579.724	76	580
473		565.697	72	566
474		551.670	78	552

TABLE 1-continued

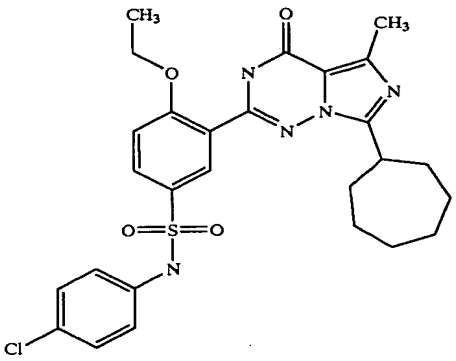
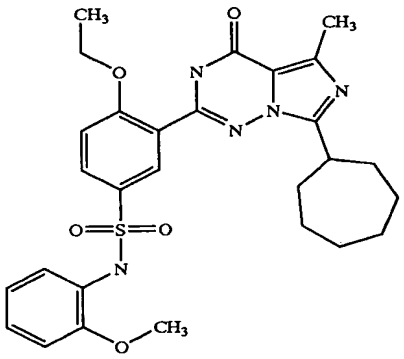
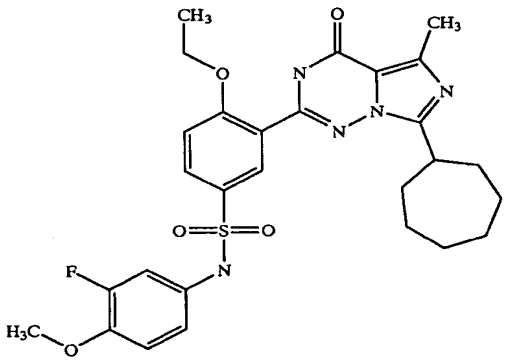
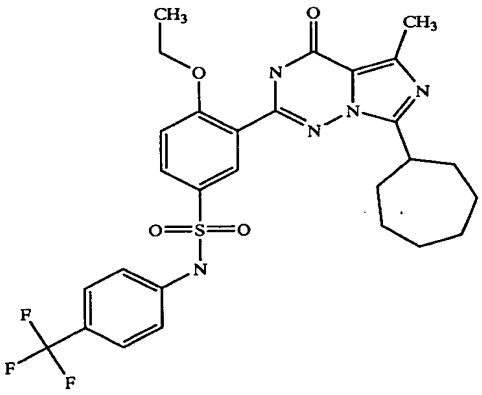
475		556.088	67	556
476		551.670	79	552
477		569.660	77	570
478		589.642	62	590

TABLE 1-continued

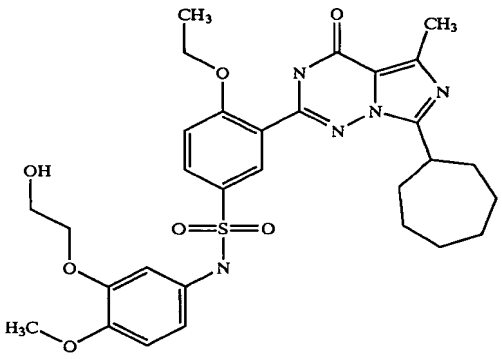
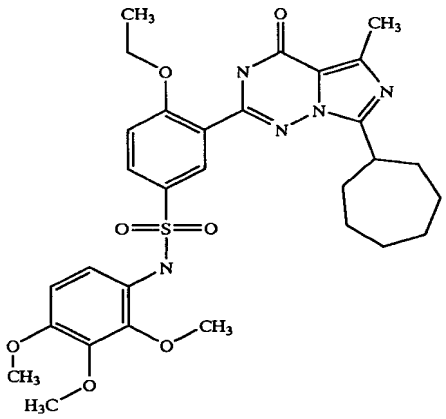
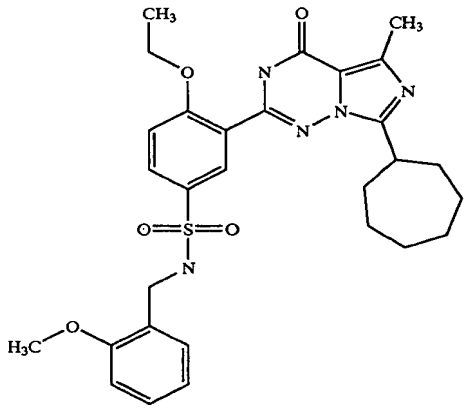
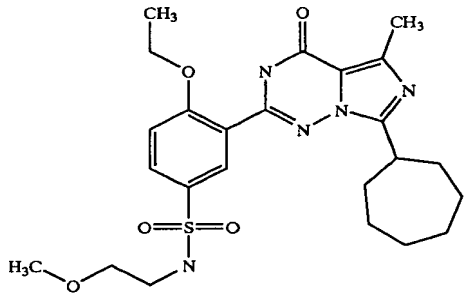
479		611.723	66	612
480		611.723	86	612
481		565.697	80	566
482		503.625	85	504

TABLE 1-continued

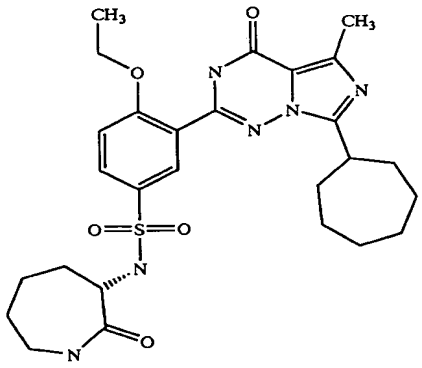
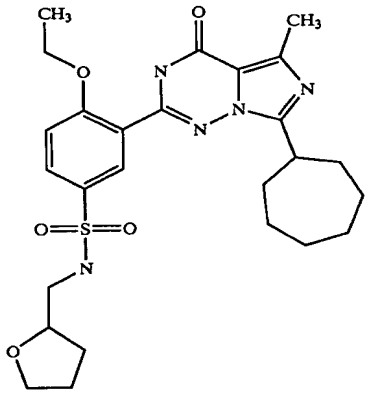
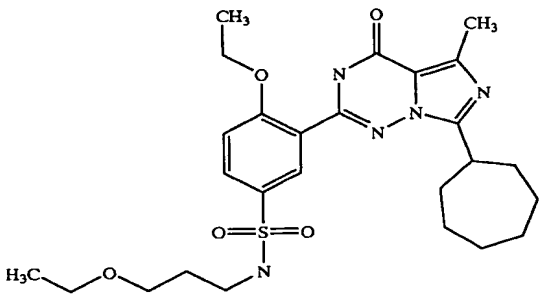
483		556.689	88	557
484		529.663	81	530
485		531.679	86	532

TABLE 1-continued

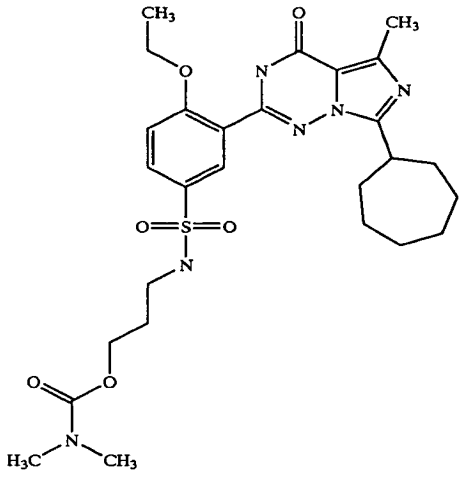
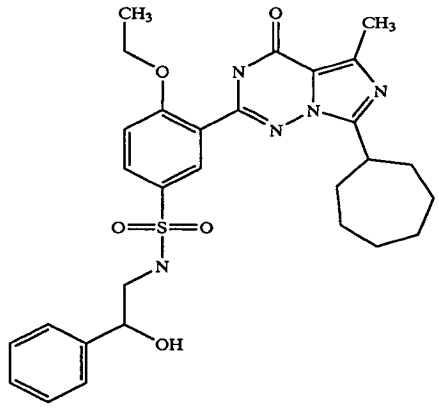
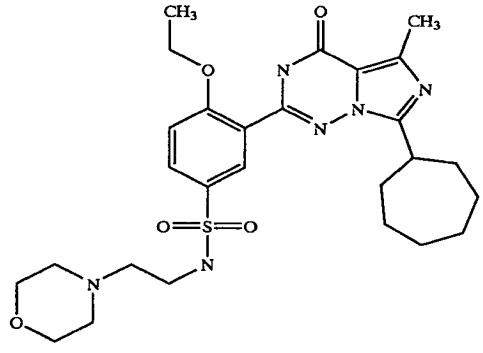
486		574.705	33	575
487		565.697	61	566
488		558.705	47	559

TABLE 1-continued

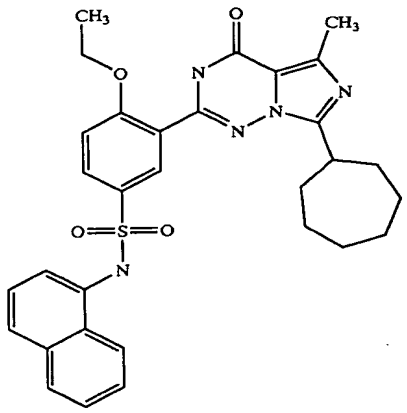
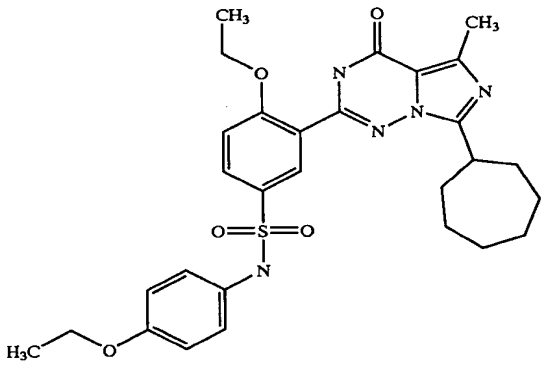
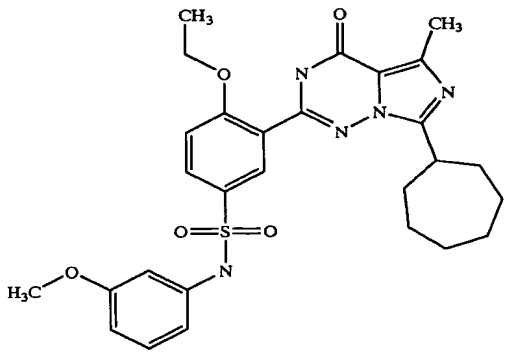
489		571.704	59	572
490		565.697	70	566
491		551.670	65	552

TABLE 1-continued

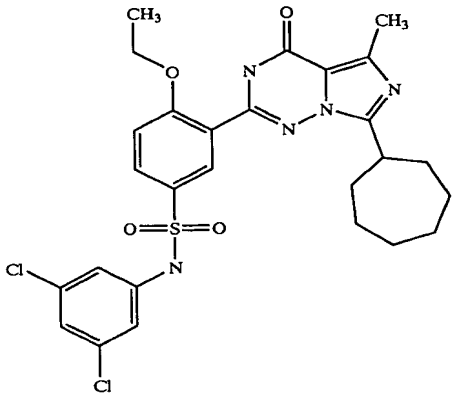
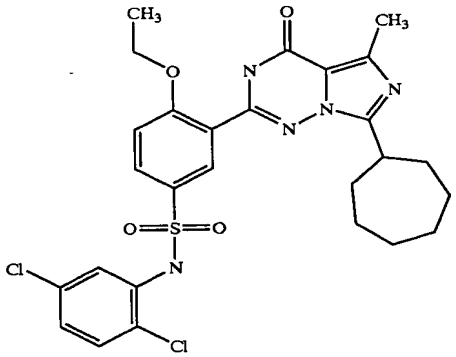
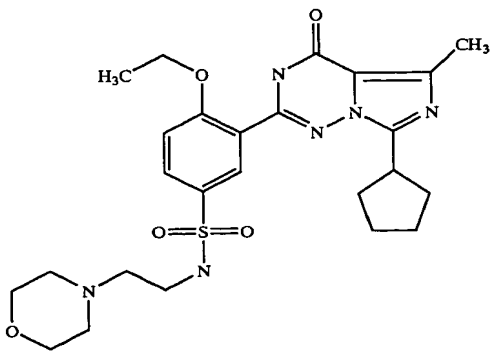
492		590.533	46	590
493		590.533	83	590
494		530.65	82	531

TABLE 1-continued

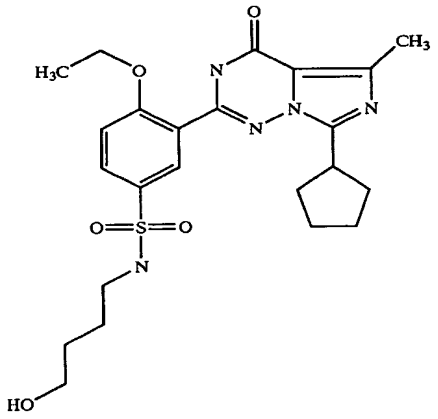
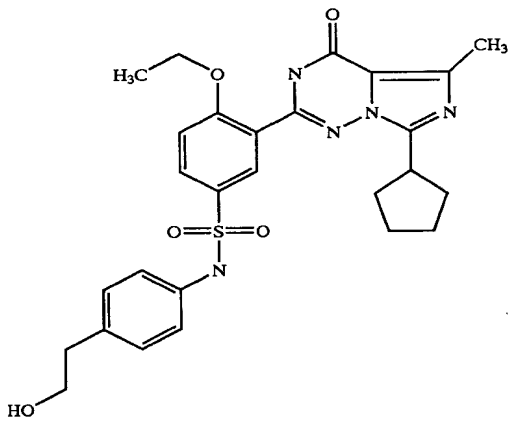
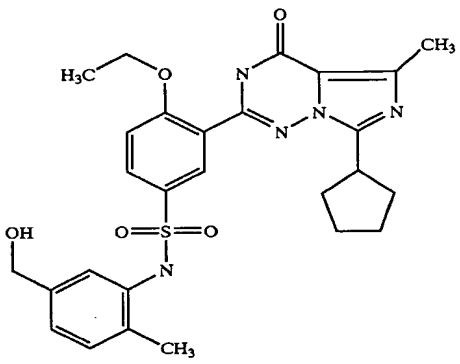
495		489.60	49	490
496		537.64	63	538
497		537.64	44	538

TABLE 1-continued

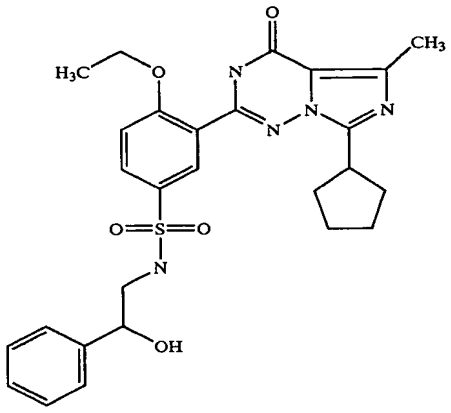
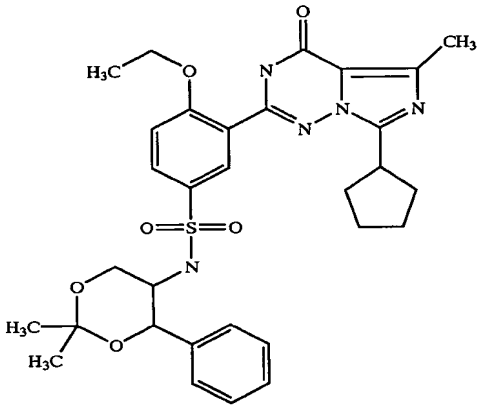
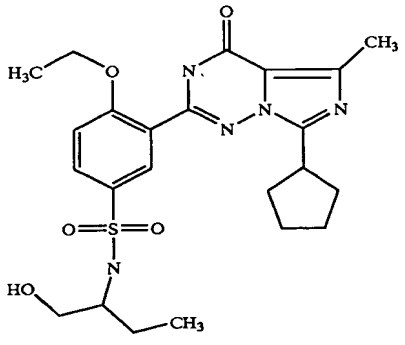
498		537.64	72	538
499		607.73	50	608
500		489.60	64	490

TABLE 1-continued

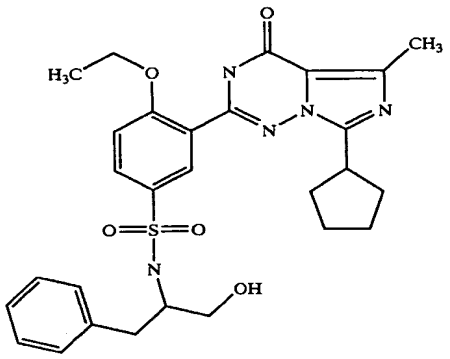
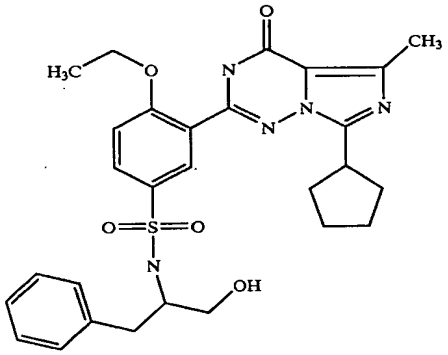
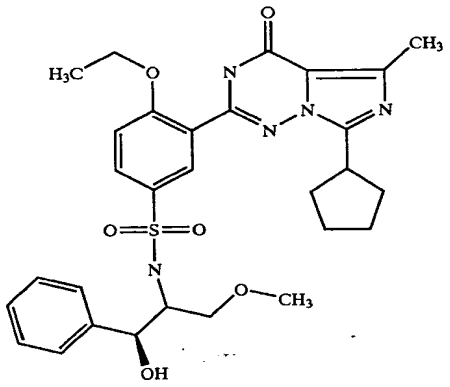
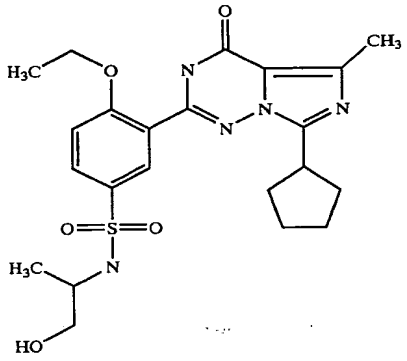
501		551.67	70	552
502		551.67	77	552
503		581.70	85	582
504		475.57	45	476

TABLE 1-continued

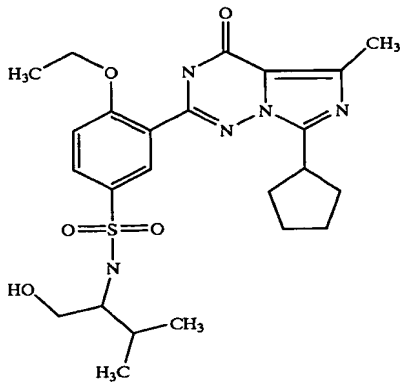
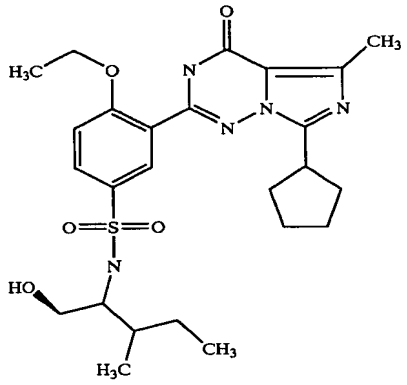
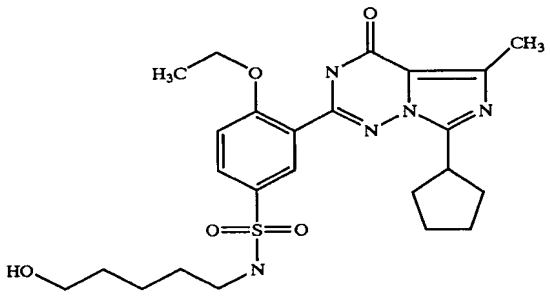
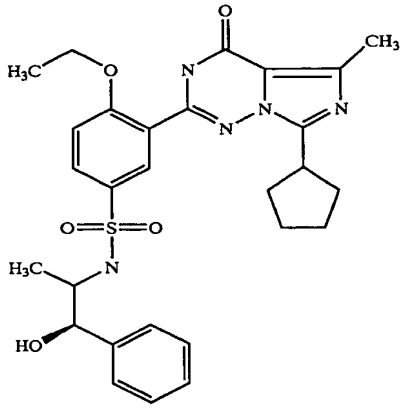
505		503.63	74	504
506		517.65	76	518
507		503.63	59	504
508		551.67	74	552

TABLE 1-continued

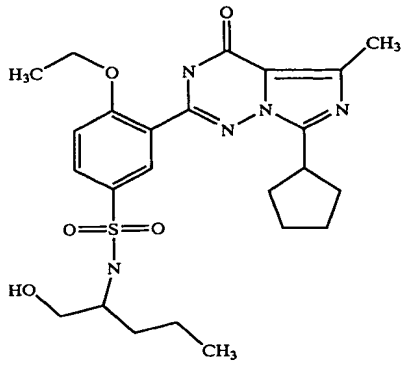
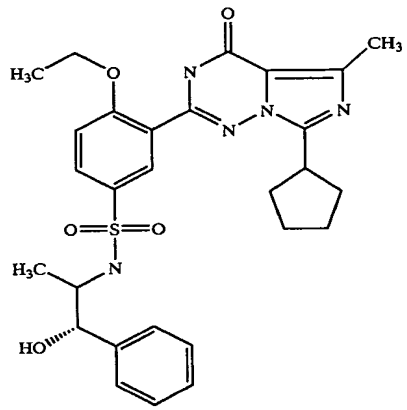
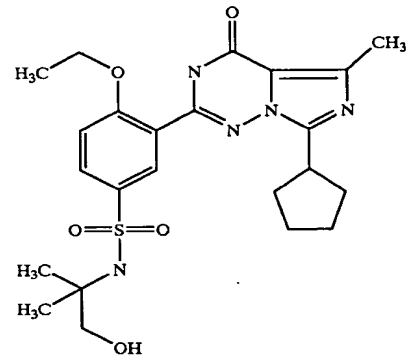
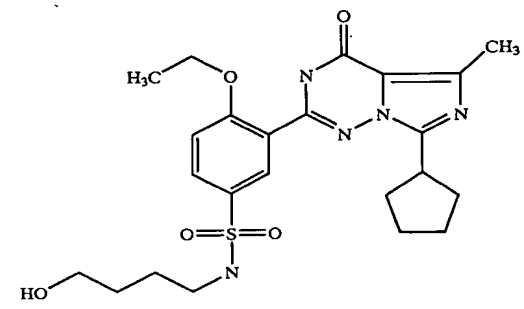
509		503.63	70	504
510		551.67	73	552
511		489.60	57	490
512		489.60	44	490

TABLE 1-continued

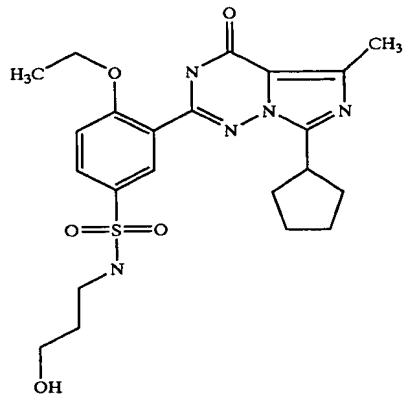
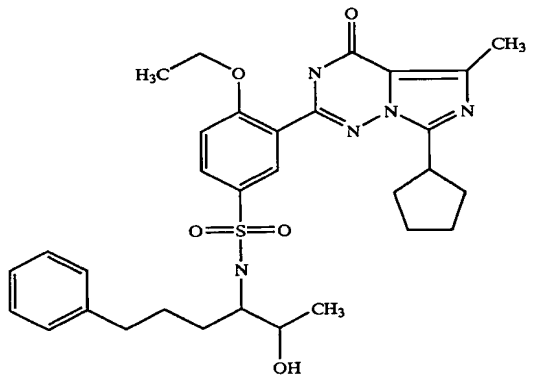
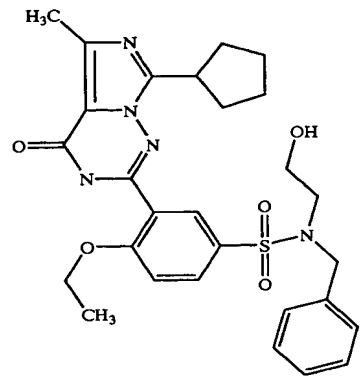
513		475.57	42	476
514		593.75	68	594
515		551.67	77	552

TABLE 1-continued

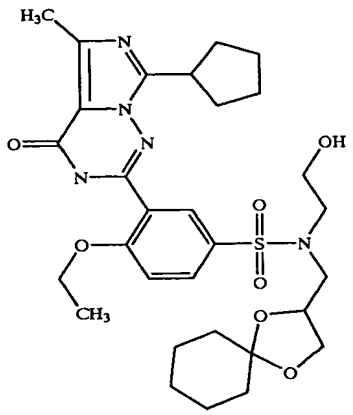
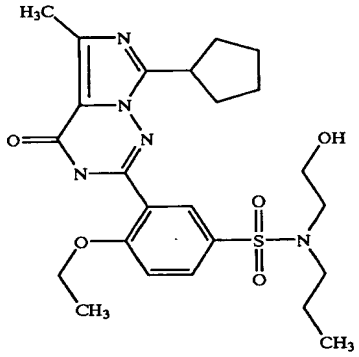
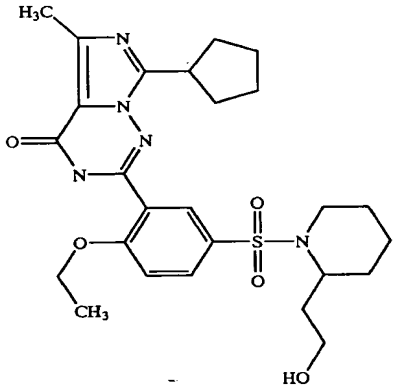
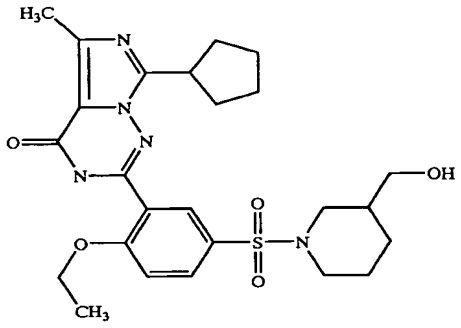
516		615.75	78	616
517		503.63	52	504
518		529.66	59	530
519		515.64	50	516

TABLE 1-continued

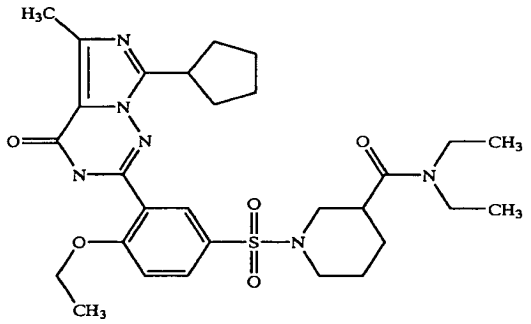
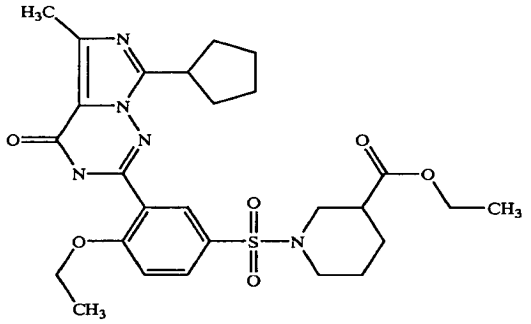
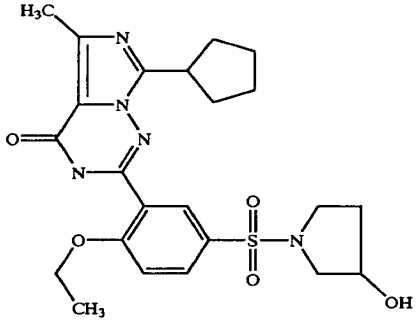
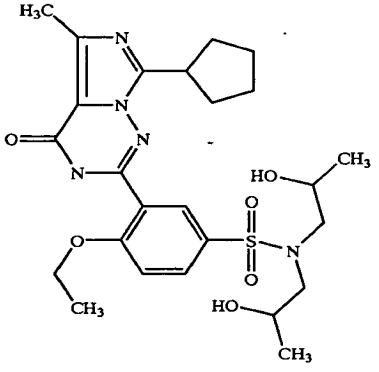
520		584.74	42	585
521		557.67	82	558
522		487.58	30	488
523		533.65	60	534

TABLE 1-continued

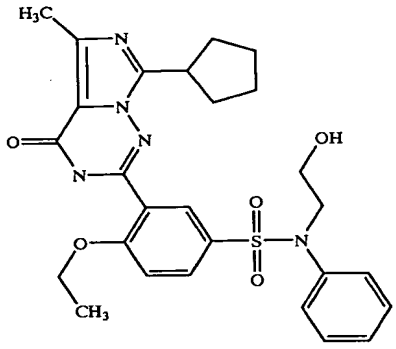
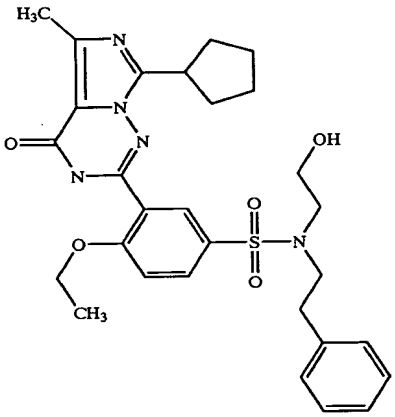
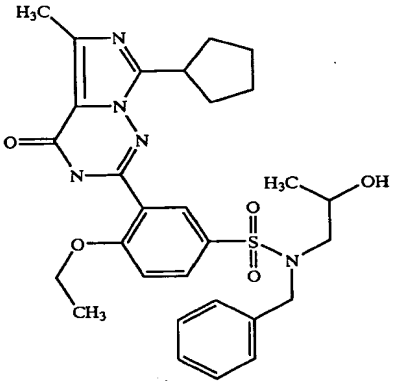
524		537.64	81	538
525		565.70	82	566
526		565.70	56	566

TABLE 1-continued

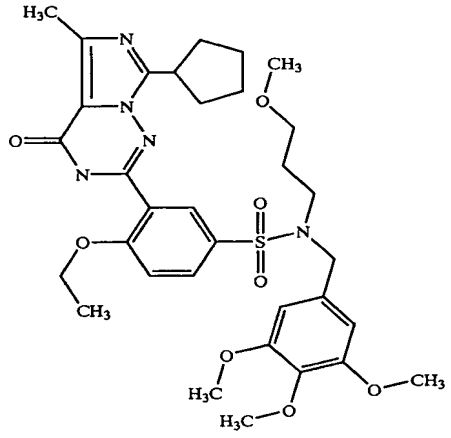
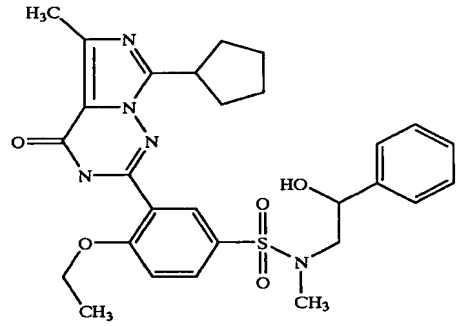
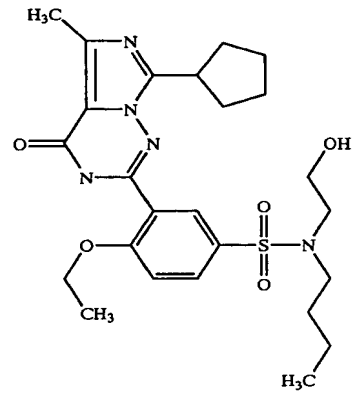
527		669.80	82	670
528		551.67	77	552
529		517.65	91	518

TABLE 1-continued

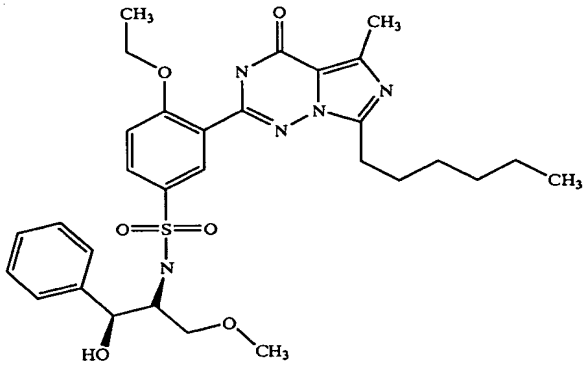
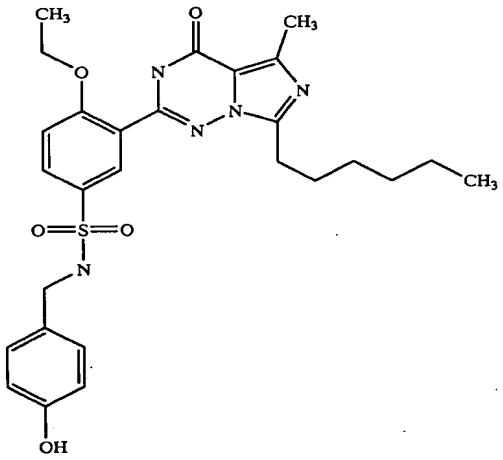
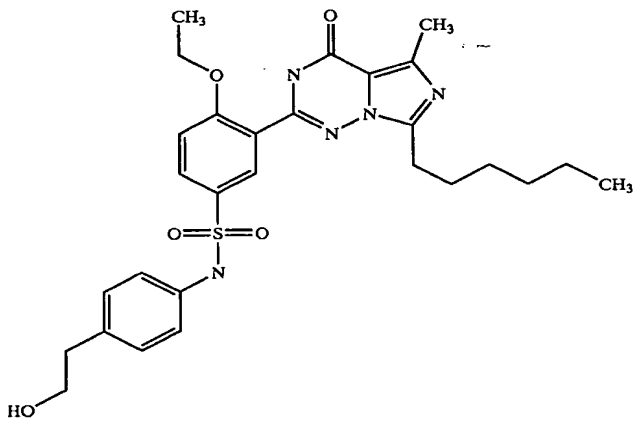
530		597.7392	84	598
531		539.6586	74	540
532		553.6857	77	554

TABLE 1-continued

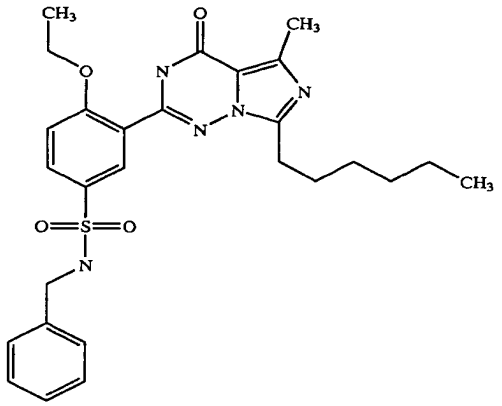
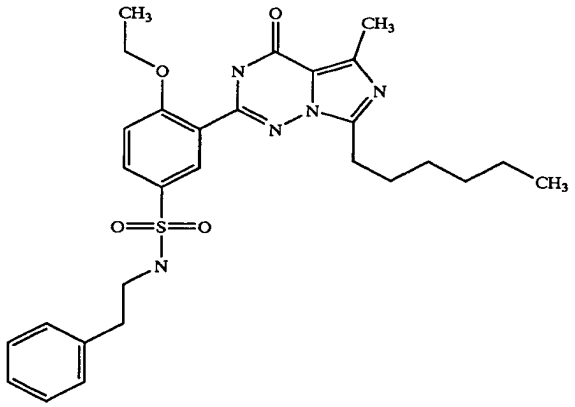
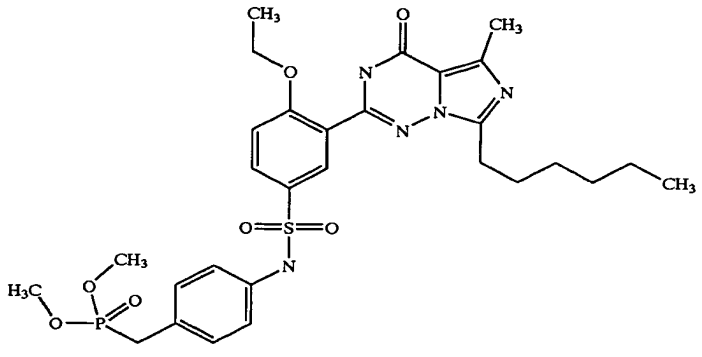
533		523.6592	93	524
534		537.6863	94	538
535		659.74	89	660

TABLE 1-continued

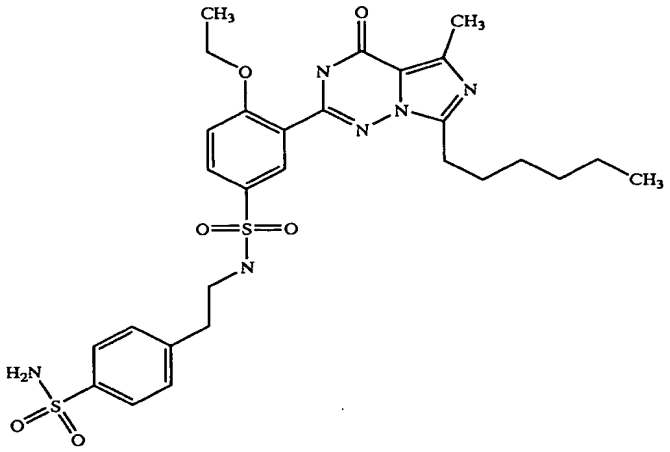
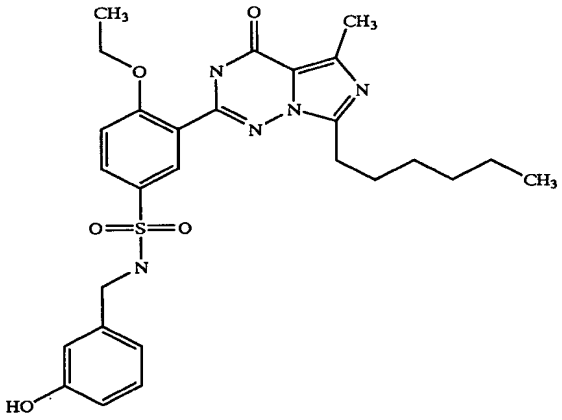
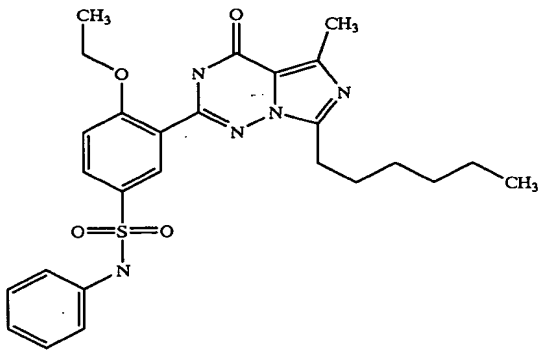
536		616.7637	80	617
537		539.6586	73	540
538		509.6321	92	510

TABLE 1-continued

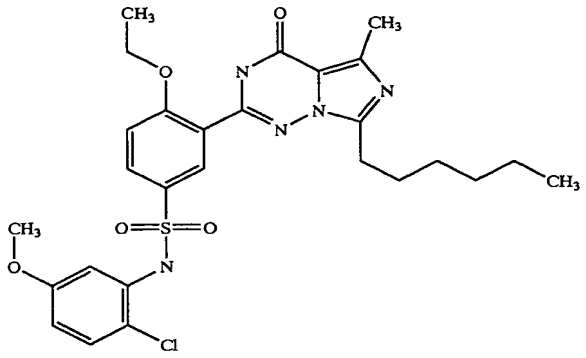
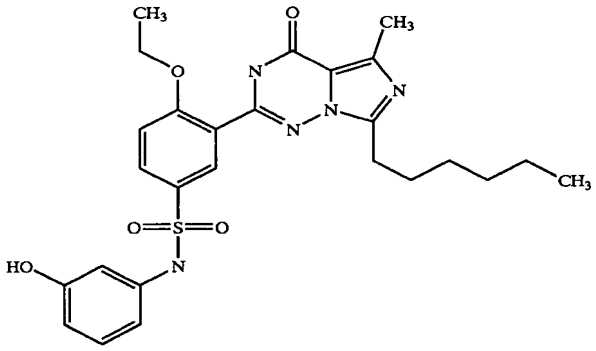
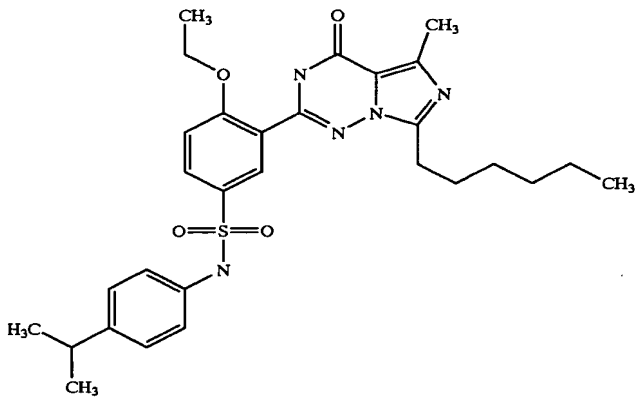
539		574.1036	48	574
540		525.6315	75	526
541		551.7133	84	552

TABLE 1-continued

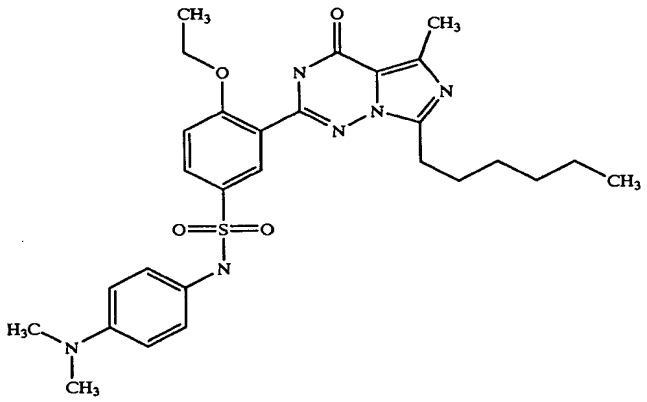
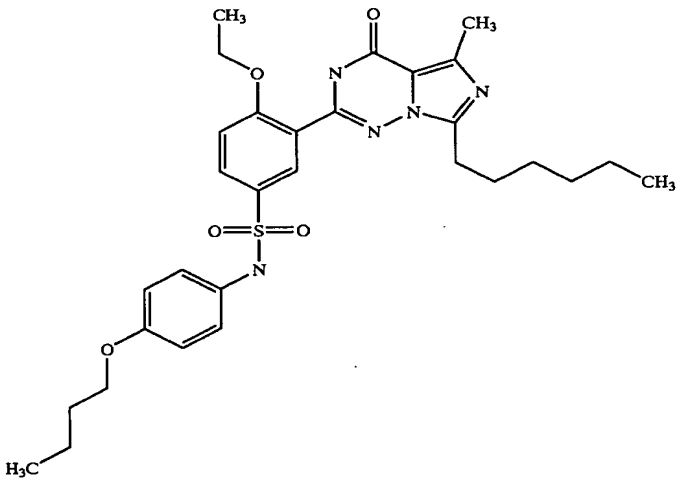
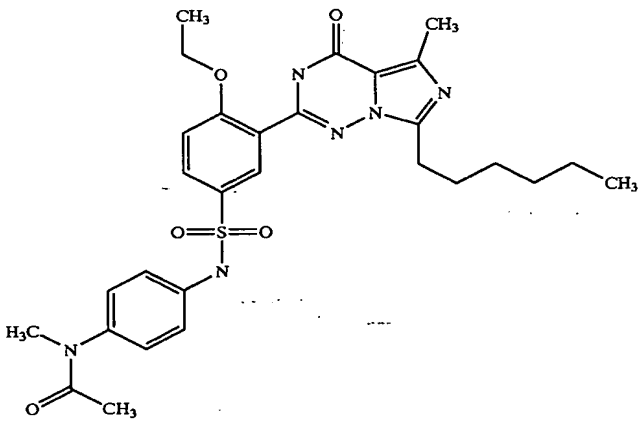
542		552.7009	75	553
543		581.7398	83	582
544		580.7115	80	581

TABLE 1-continued

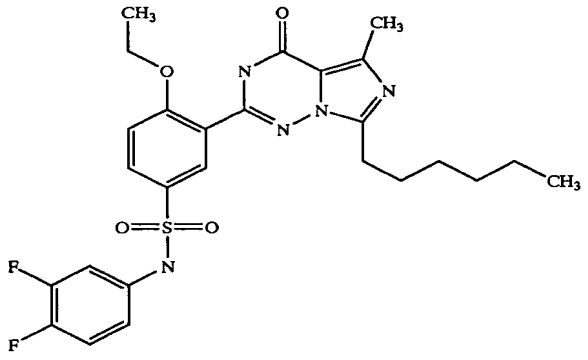
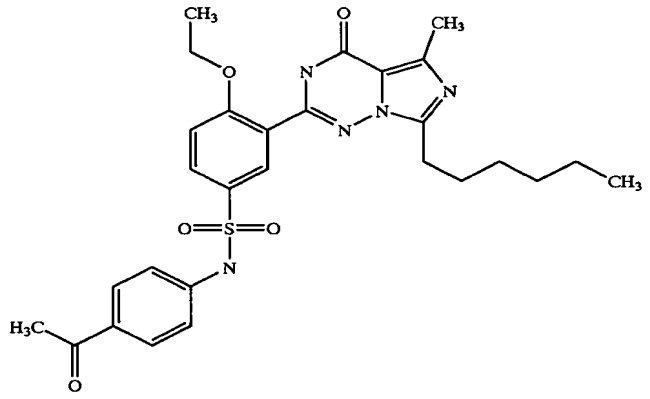
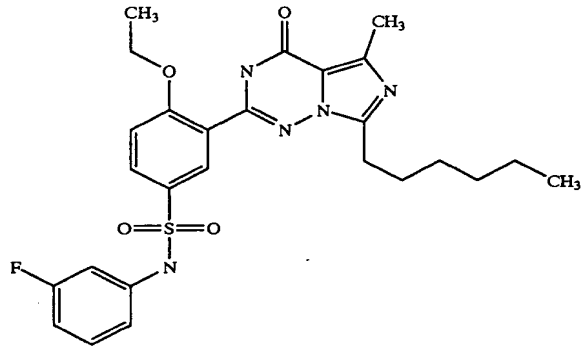
545		545.6129	91	546
546		551.6697	54	552
547		527.6225	89	528

TABLE 1-continued

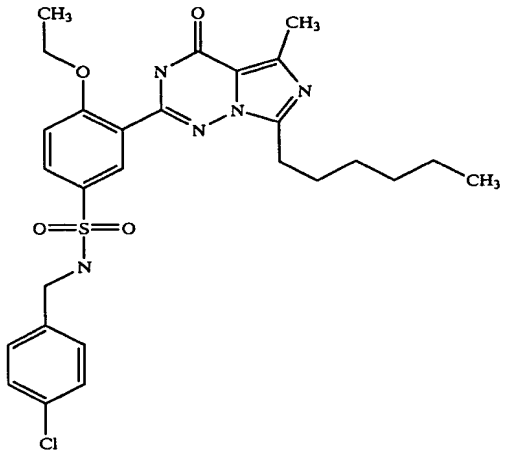
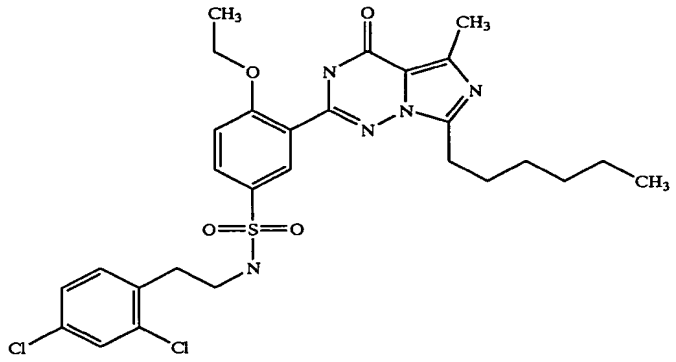
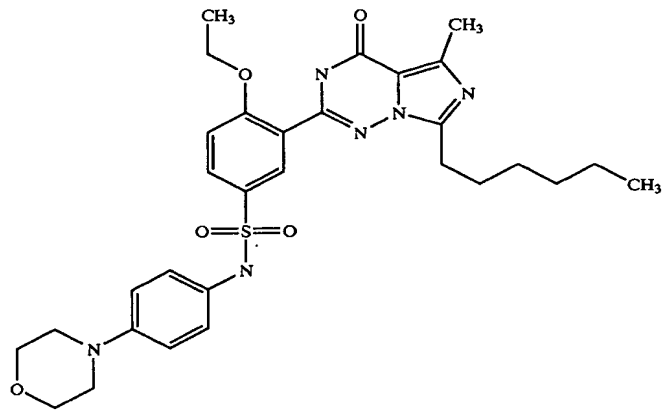
548		558.1042	83	558
549		606.5763	55	606
550		594.7386	83	595

TABLE 1-continued

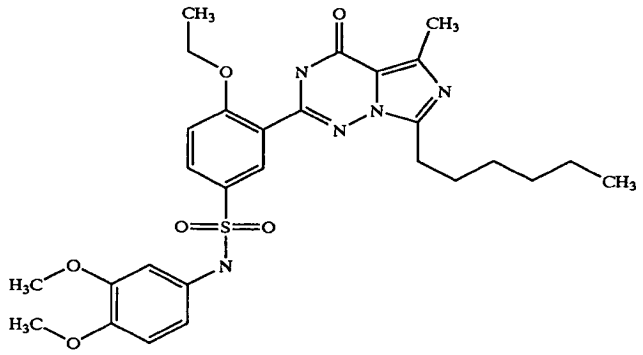
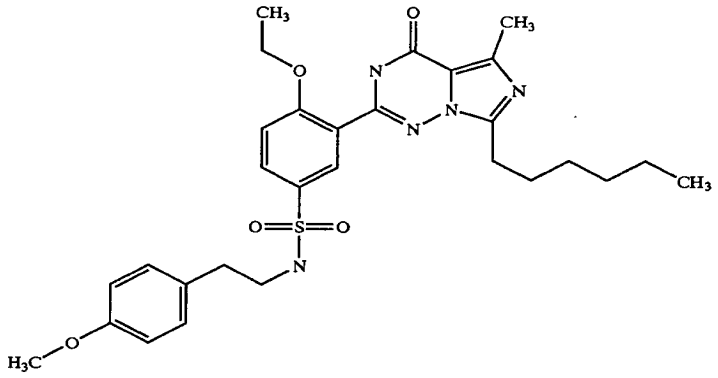
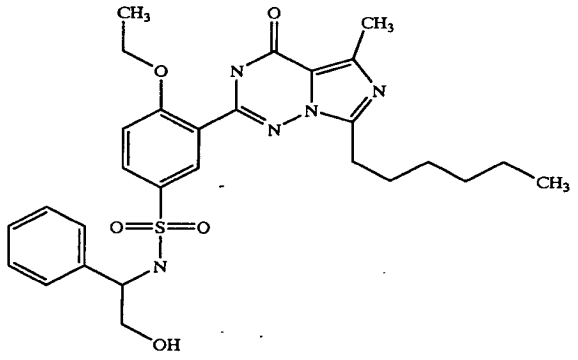
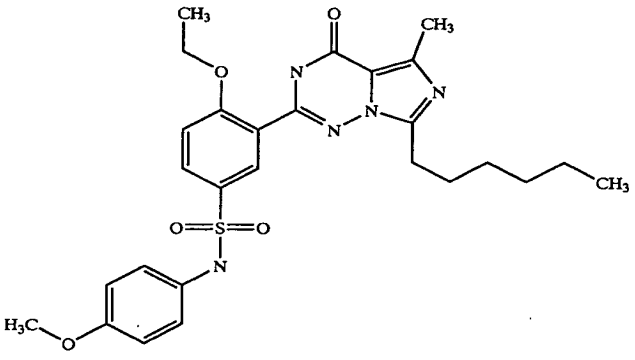
551		569.6851	87	570
552		567.7127	79	568
553		553.6857	88	554
554		539.6586	88	540

TABLE 1-continued

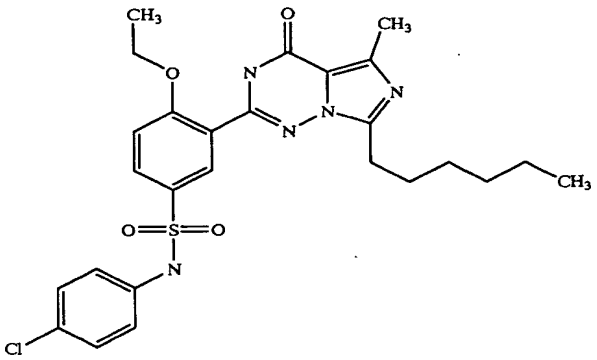
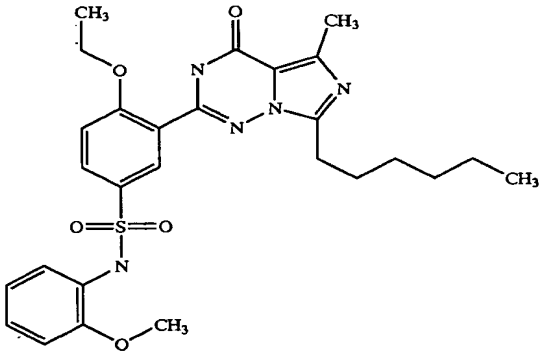
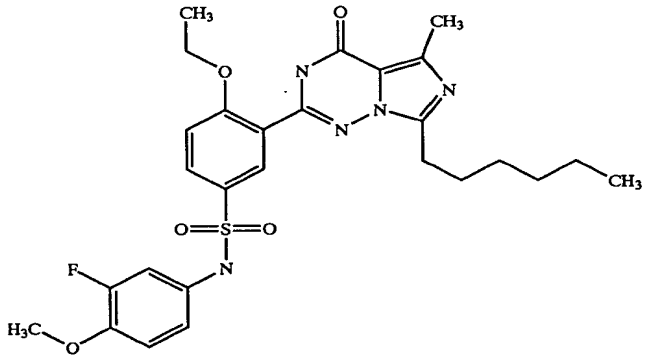
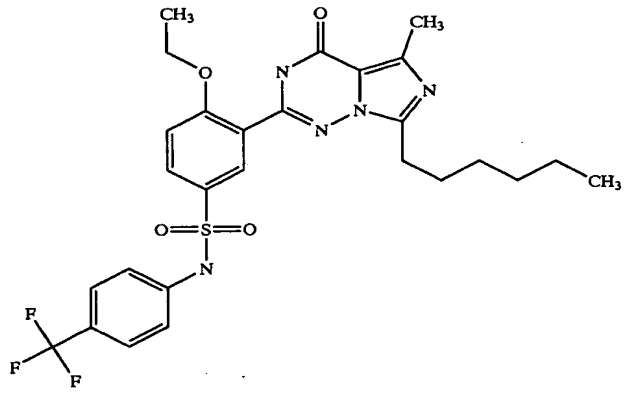
555		544.0771	83	544
556		539.6586	93	540
557		557.649	88	558
558		577.6305	77	578

TABLE 1-continued

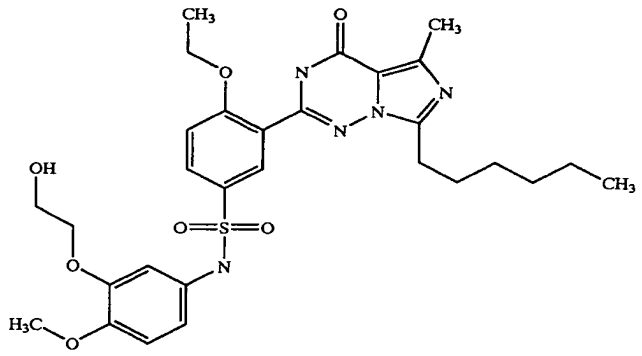
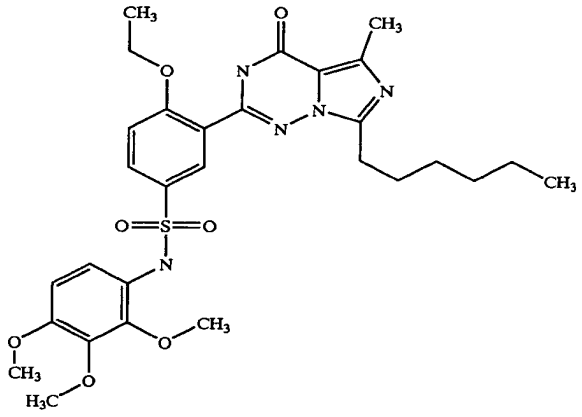
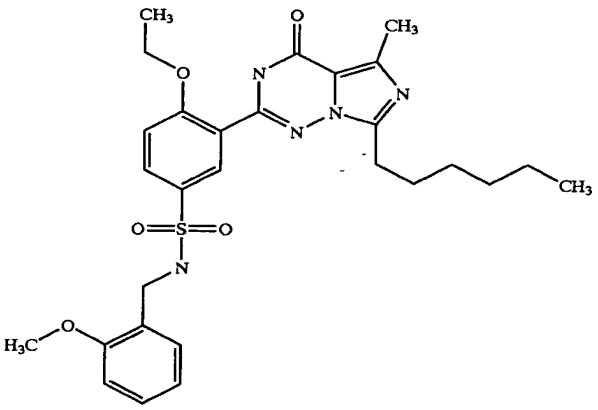
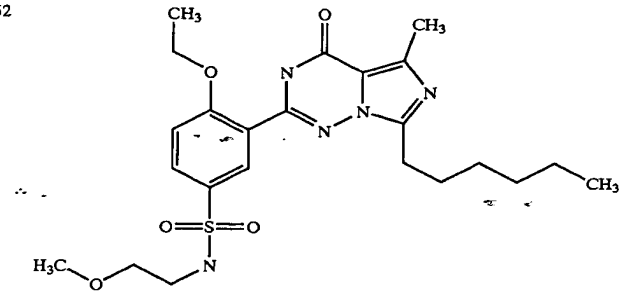
559		599.7115	81	600
560		599.7115	88	600
561		553.6857	89	554
562		491.614	92	492

TABLE 1-continued

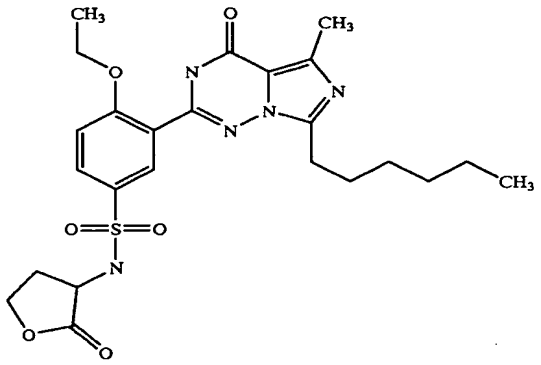
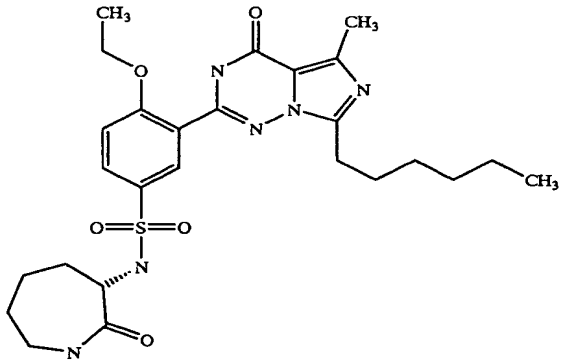
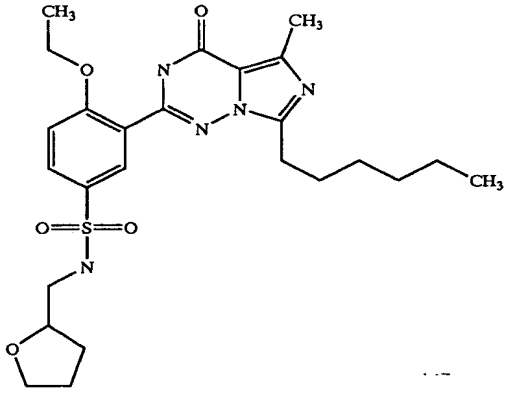
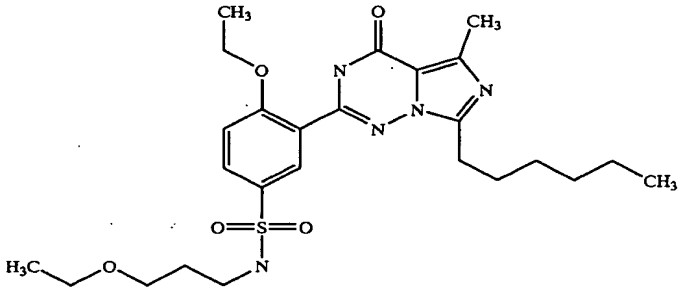
563		517.6086	83	518
564		544.678	94	545
565		517.6522	94	518
566		519.6681	95	520

TABLE 1-continued

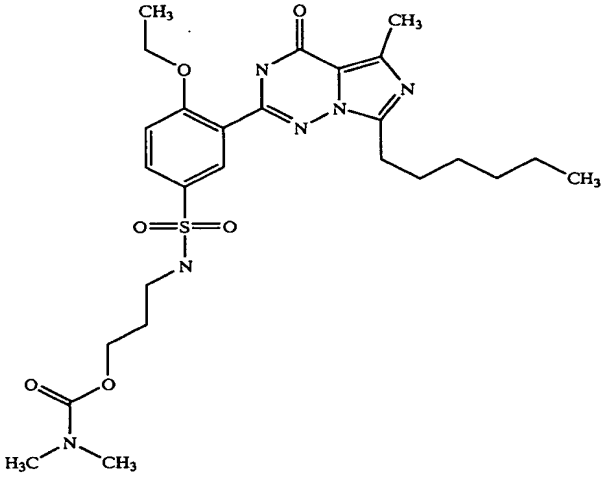
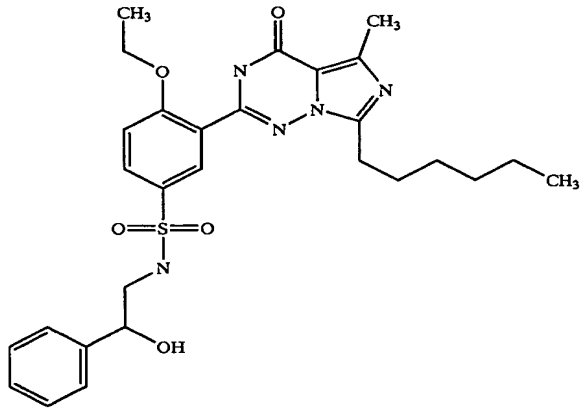
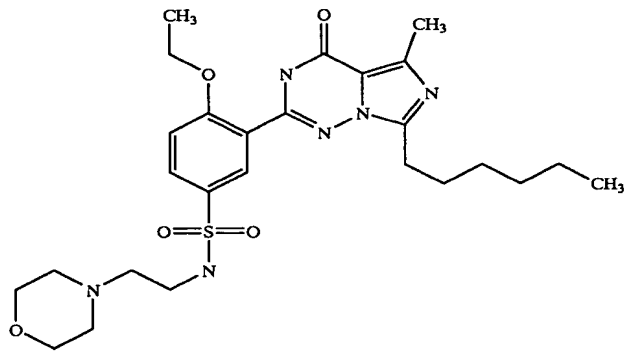
567		562.6934	74	563
568		553.6857	80	554
569		546.694	87	547

TABLE 1-continued

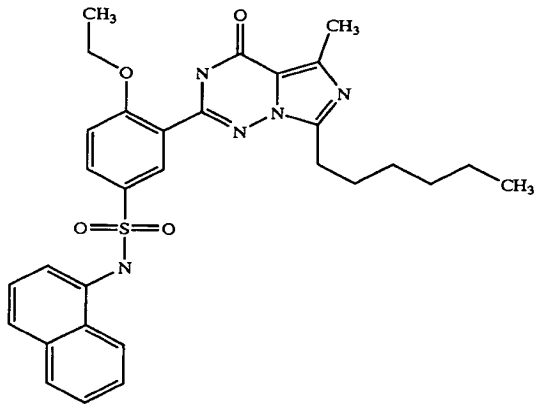
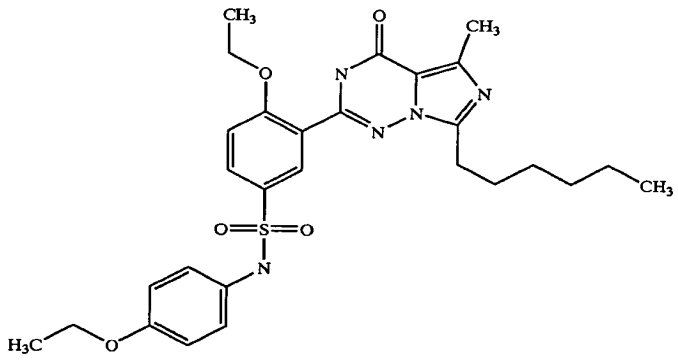
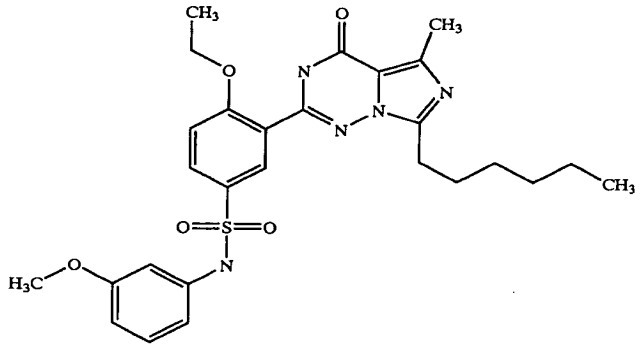
570		559.6926	73	560
571		553.6857	86	554
572		539.6586	90	540

TABLE 1-continued

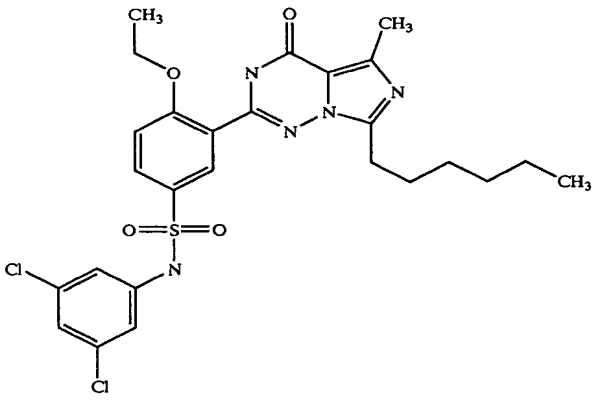
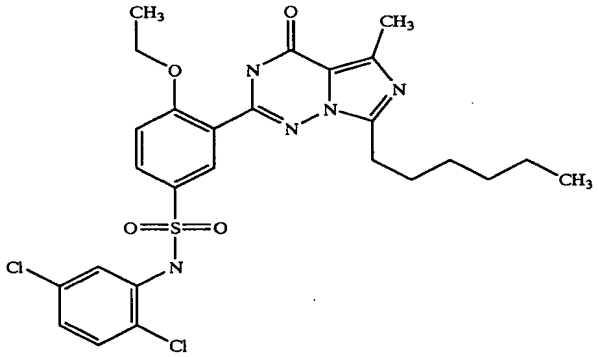
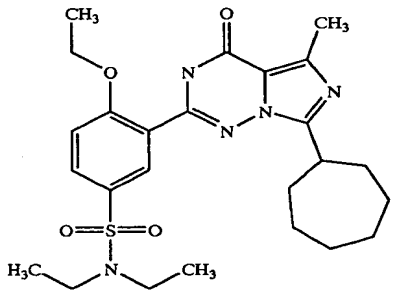
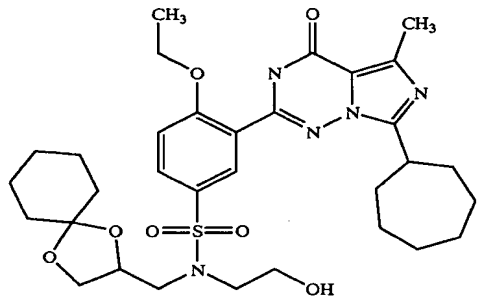
573		578.5221	87	578
574		578.5221	92	578
575		501.6528	50	502
576		643.80875	76	644

TABLE 1-continued

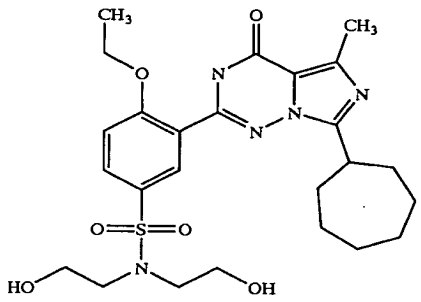
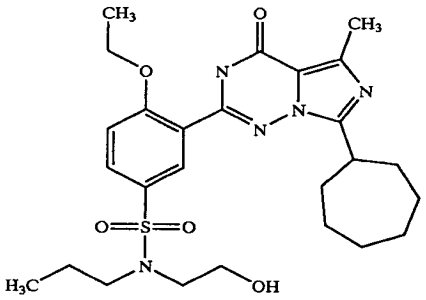
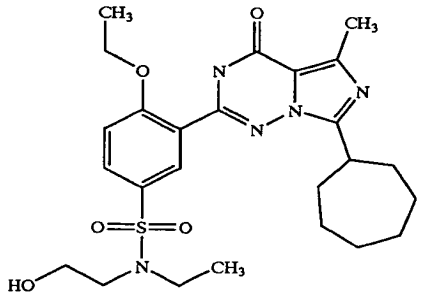
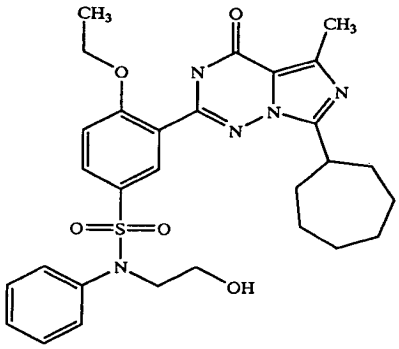
577		533.6516	75	534
578		531.67929	88	532
579		517.6522	87	518
580		565.6968	84	566

TABLE 1-continued

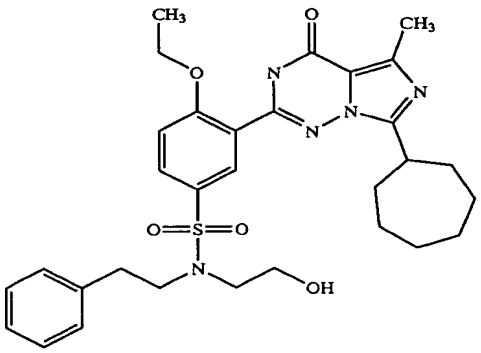
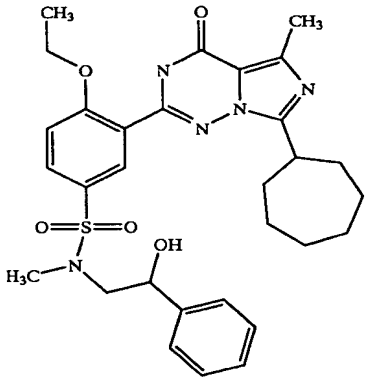
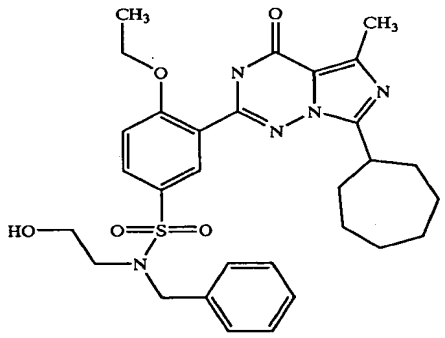
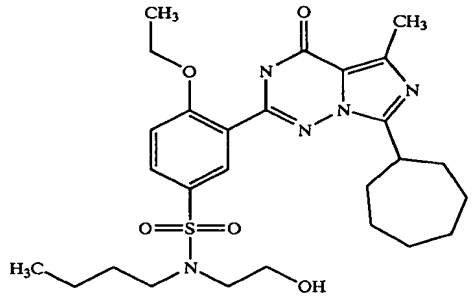
581		593.75098	88	594
582		579.72389	74	580
583		579.72389	65	580
584		545.70638	85	546

TABLE 1-continued

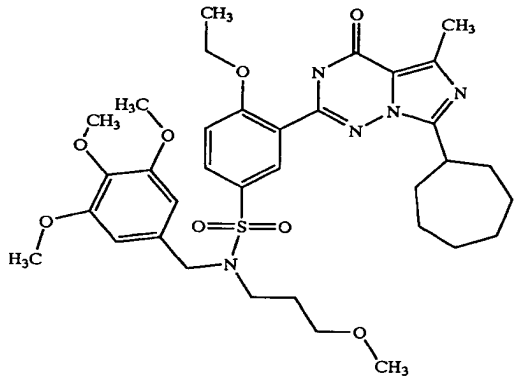
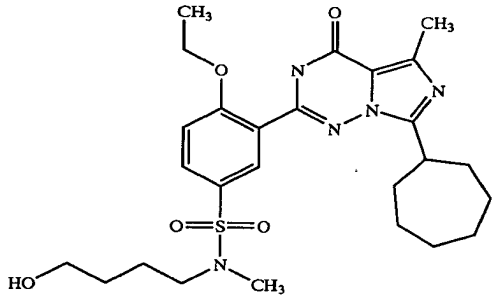
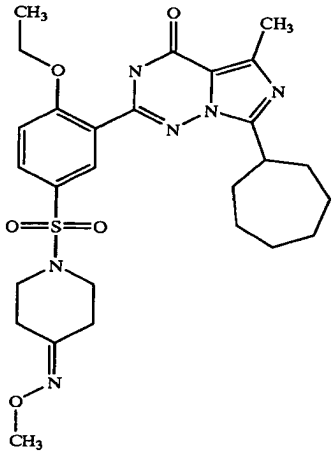
585		697.85754	68	698
586		531.67929	52	532
587		556.68917	88	557

TABLE 1-continued

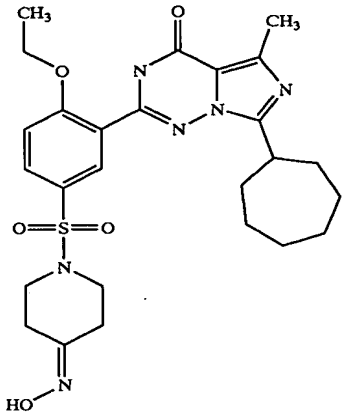
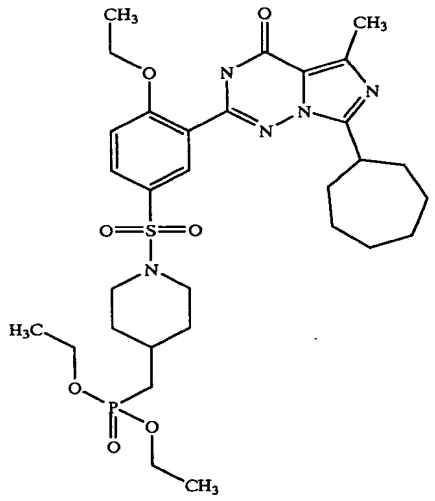
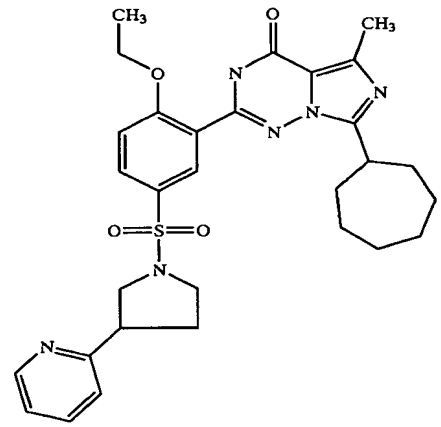
588		542.66208	78	543
589		663.77937	92	664
590		576.72322	85	577

TABLE 1-continued

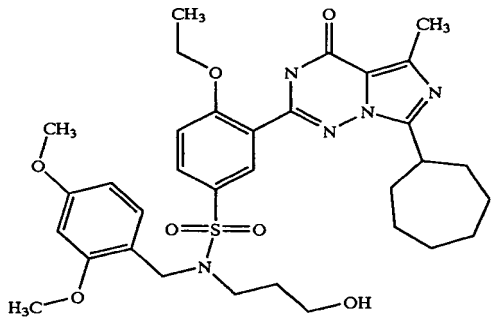
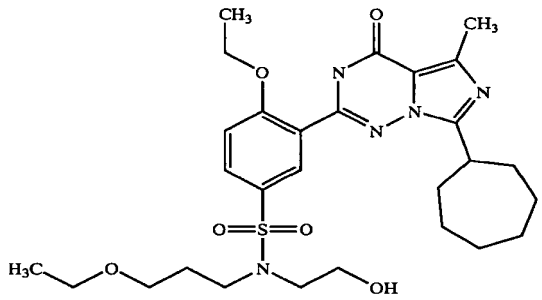
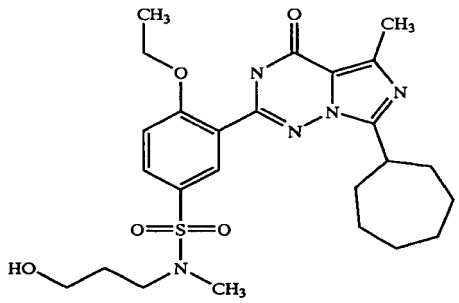
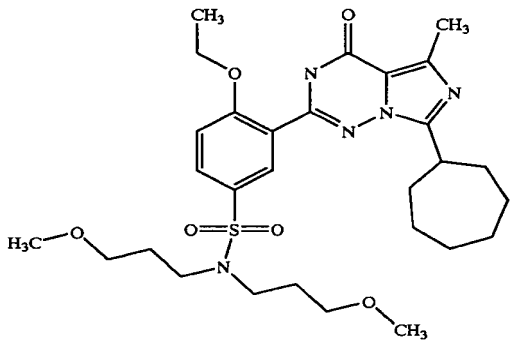
591		653.80396	77	654
592		575.73287	91	576
593		517.6522	86	518
594		589.75996	90	590

TABLE 1-continued

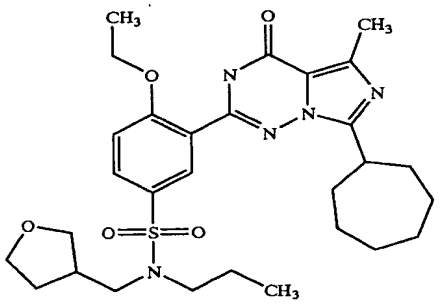
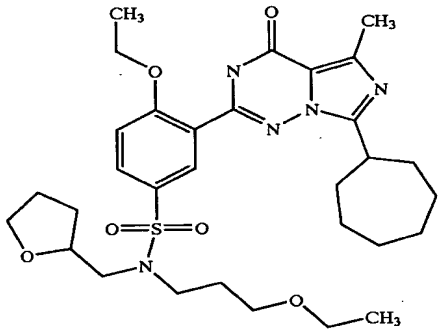
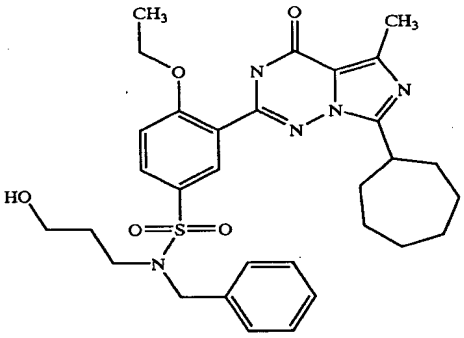
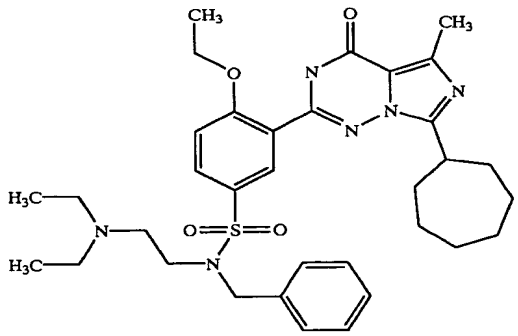
595		571.74462	71	572
596		615.7982	92	616
597		593.75098	78	594
598		634.84752	76	635

TABLE 1-continued

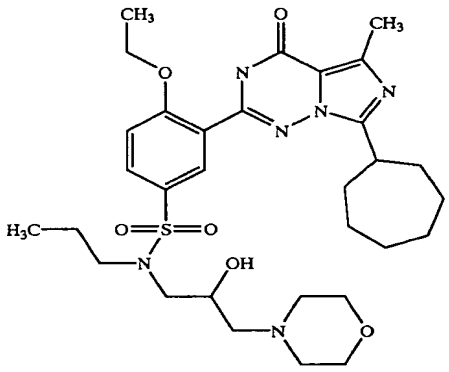
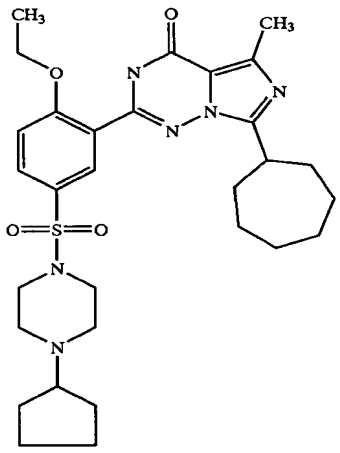
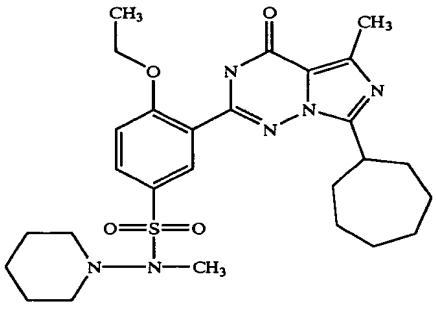
599		630.81287	81	631
600		582.77104	82	583
601		570.75989	34	571

TABLE 1-continued

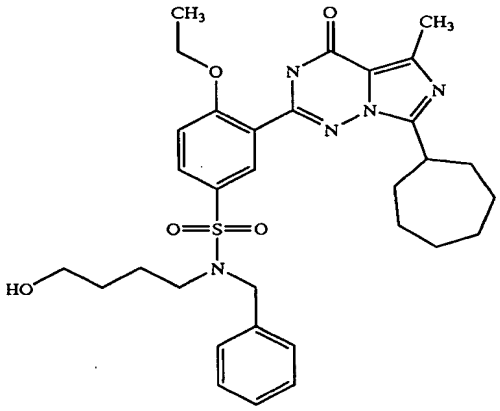
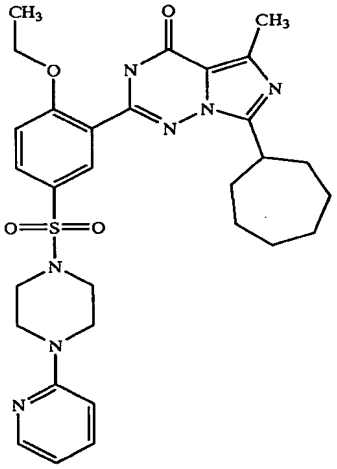
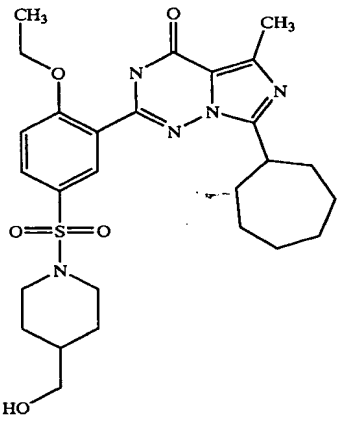
602		607.77807	82	608
603		591.73789	73	592
604		543.69044	79	544

TABLE 1-continued

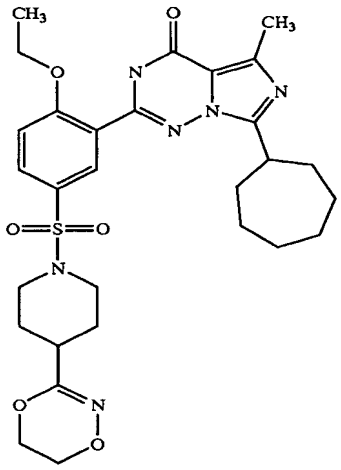
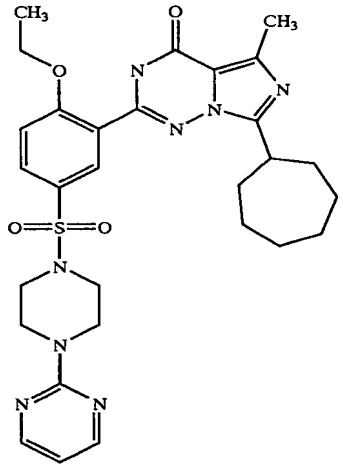
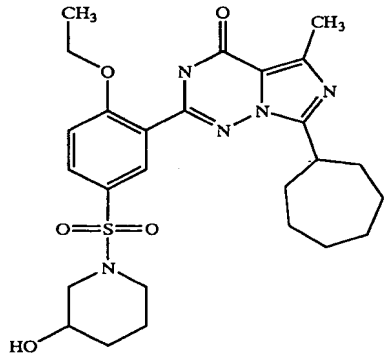
605		598.72681	68	599
606		592.72547	42	593
607		529.66335	76	530

TABLE 1-continued

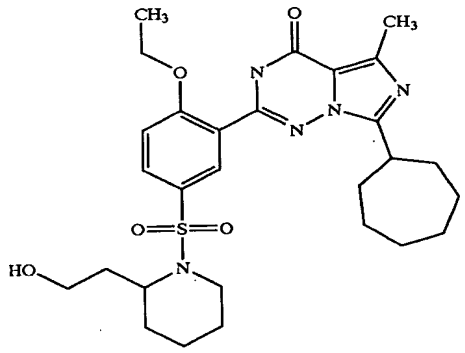
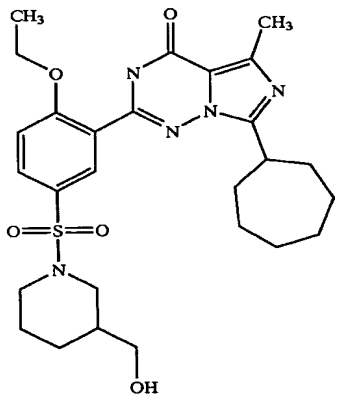
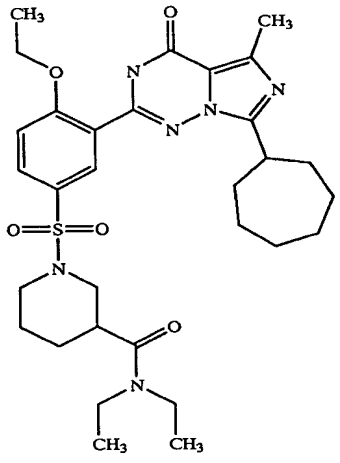
608		557.71753	88	558
609		543.69044	83	544
610		612.79753	64	613

TABLE 1-continued

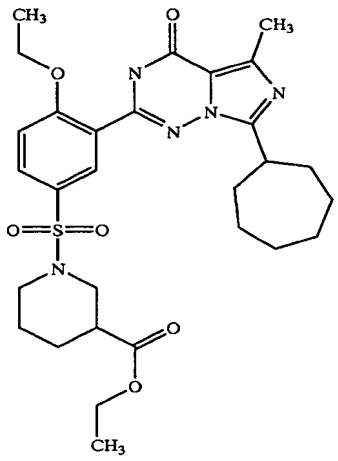
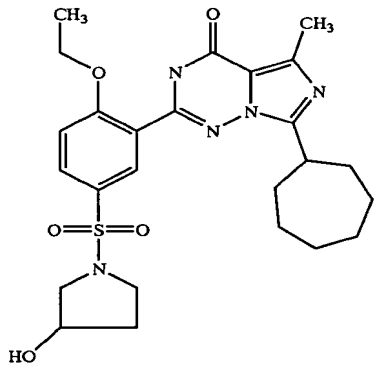
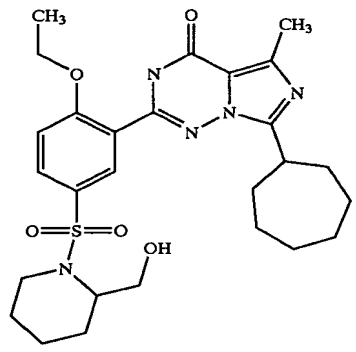
611		585.72808	88	586
612		515.63626	81	516
613		543.69044	78	544

TABLE 1-continued

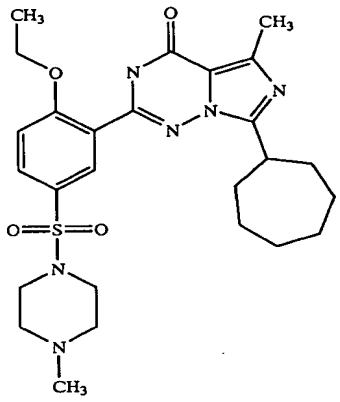
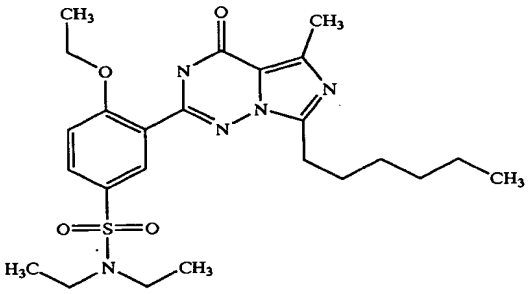
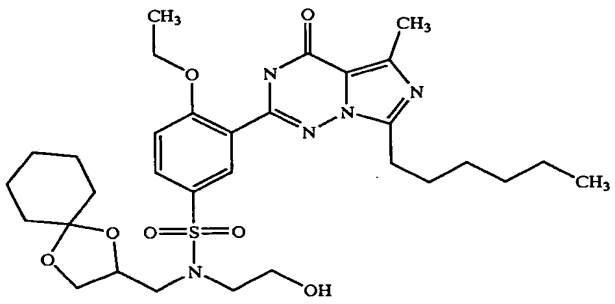
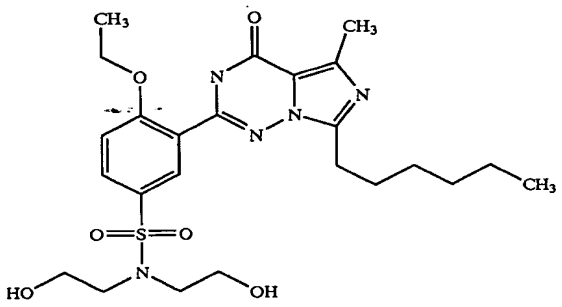
614		528.67862	30	529
615		489.64	84	490
616		631.80	88	632
617		521.64	87	522

TABLE 1-continued

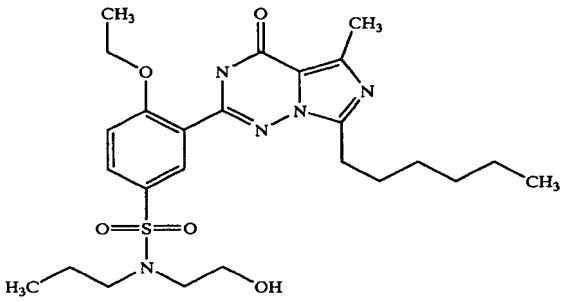
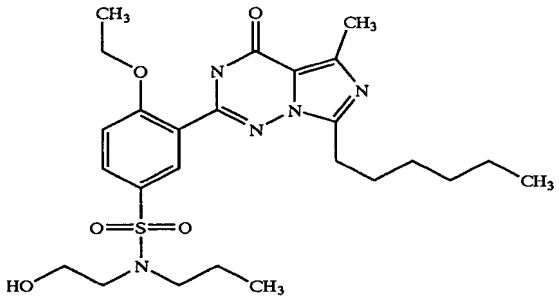
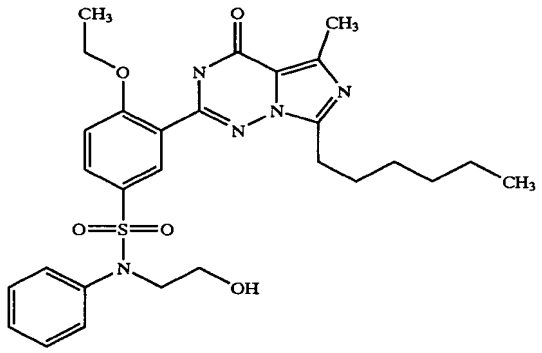
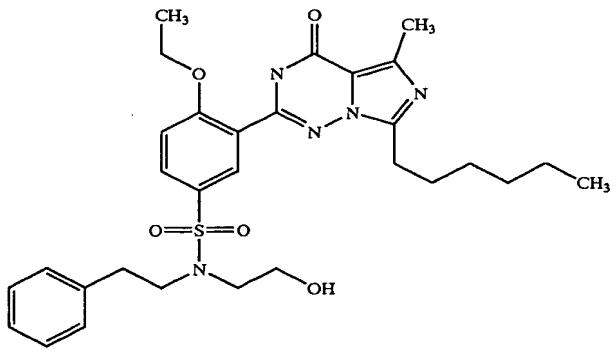
618		519.67	89	520
619		505.64	94	506
620		553.69	90	554
621		581.74	85	582

TABLE 1-continued

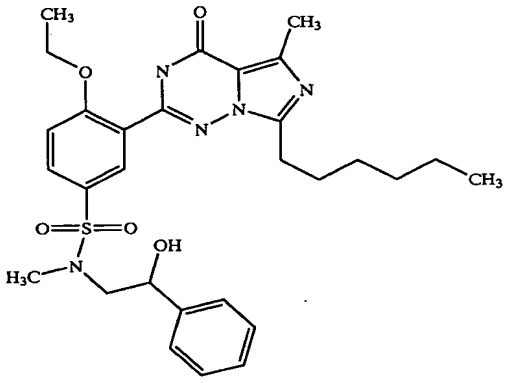
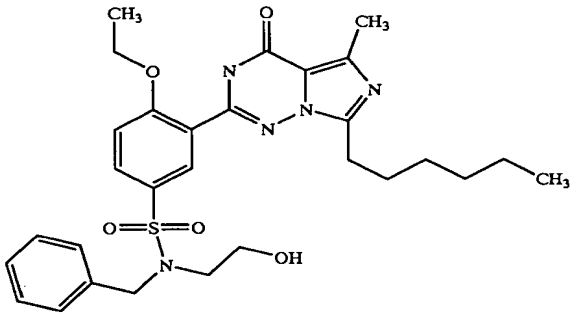
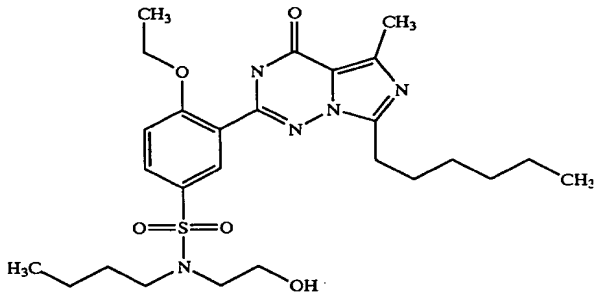
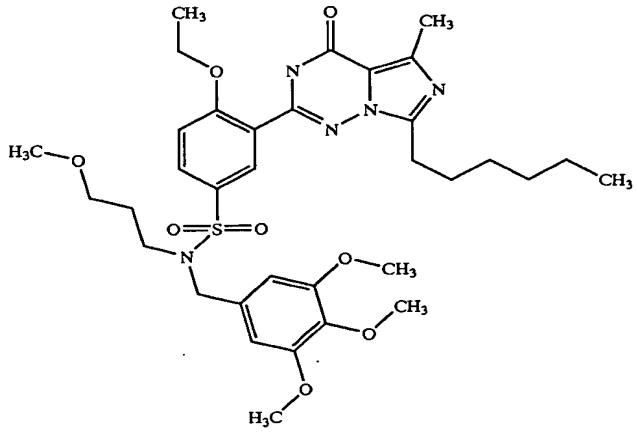
622		567.71	85	568
623		567.71	86	568
624		533.70	85	534
625		685.85	84	686

TABLE 1-continued

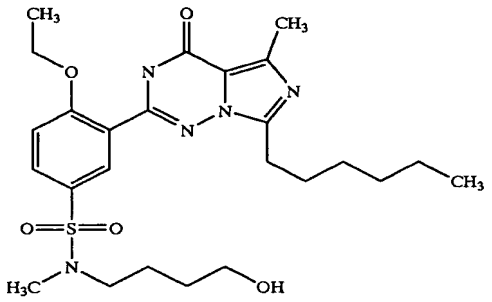
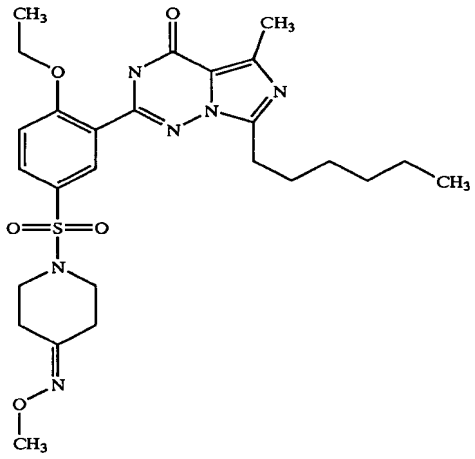
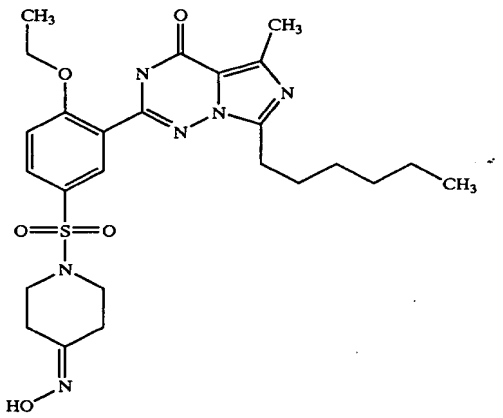
626		519.67	83	520
627		544.68	92	545
628		530.65	82	531

TABLE 1-continued

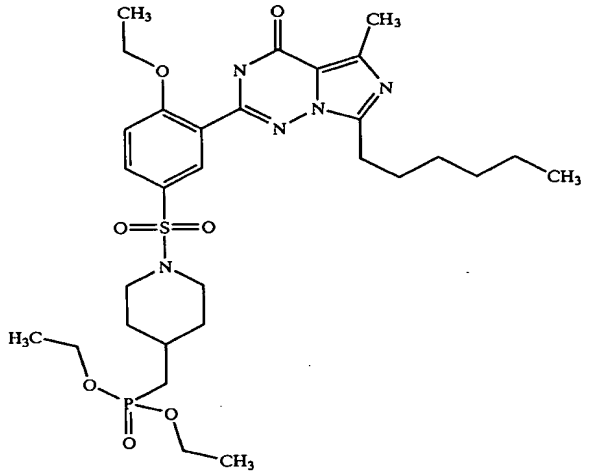
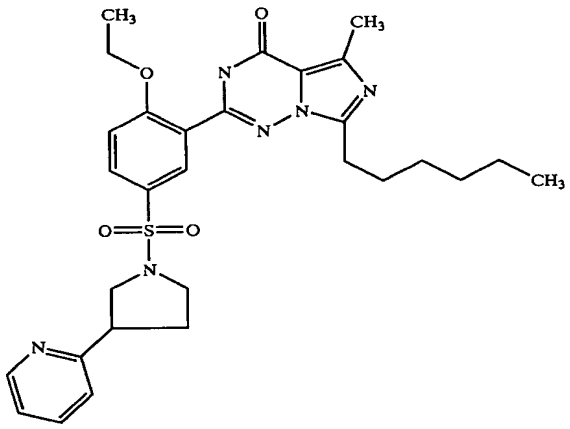
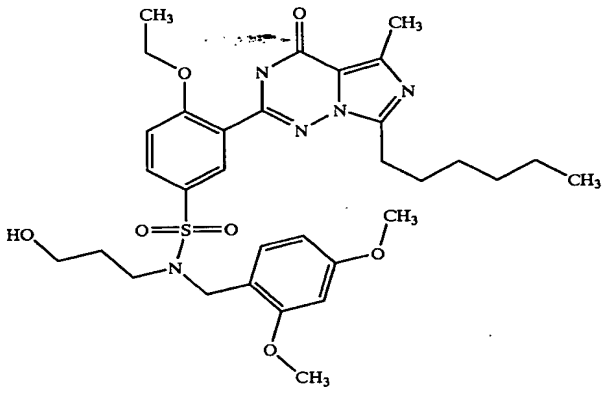
629		651.77	89	652
630		564.71	87	565
631		641.79	87	642

TABLE 1-continued

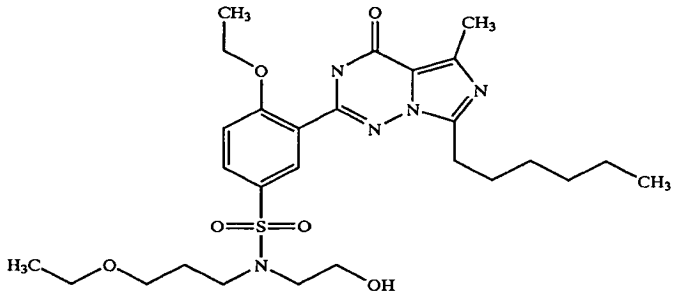
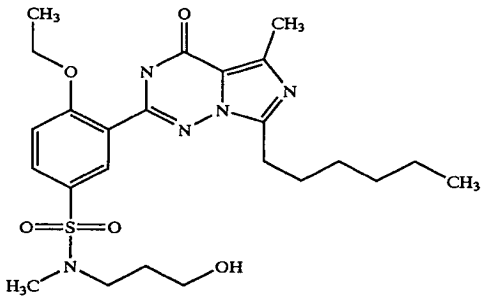
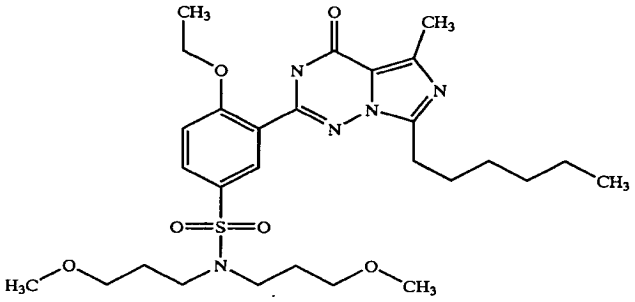
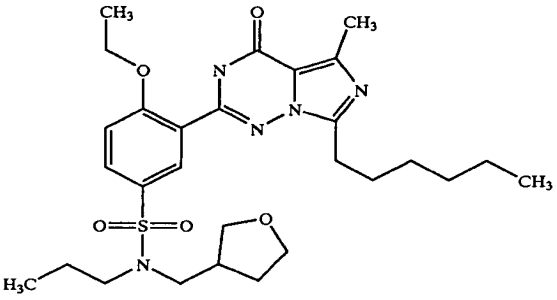
632		563.72	85	564
633		505.64	88	506
634		577.75	96	578
635		559.73	79	560

TABLE 1-continued

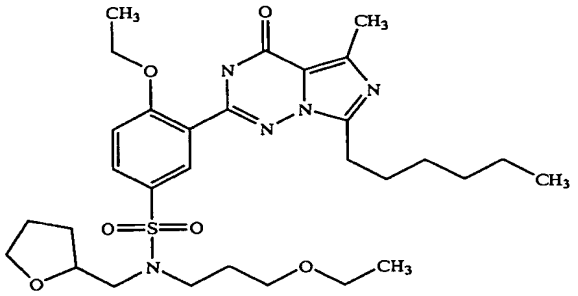
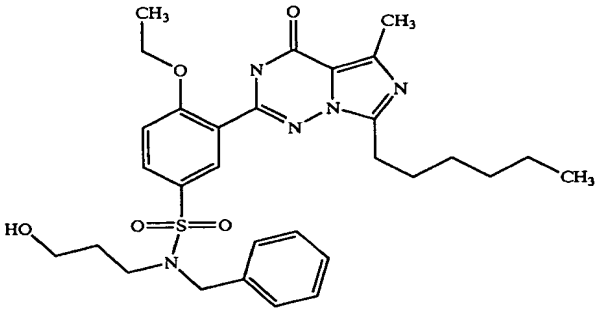
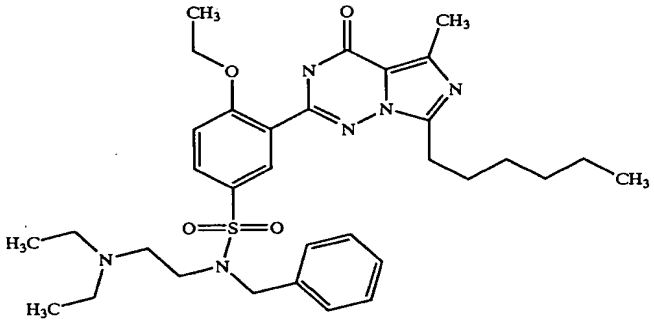
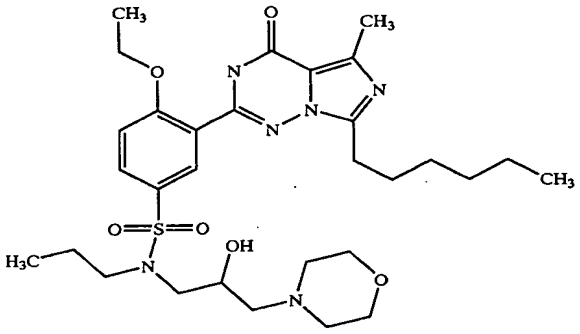
636		603.79	88	604
637		581.74	83	582
638		622.84	90	623
639		618.80	85	619

TABLE 1-continued

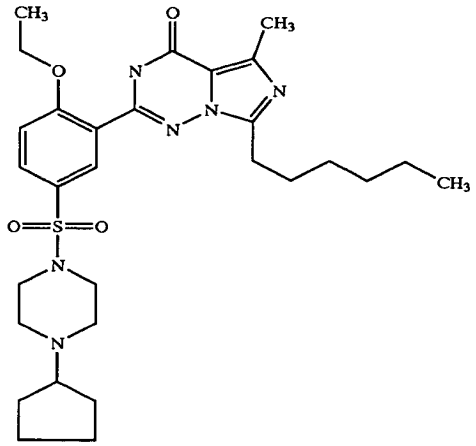
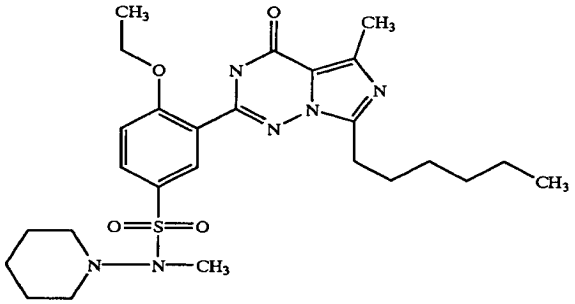
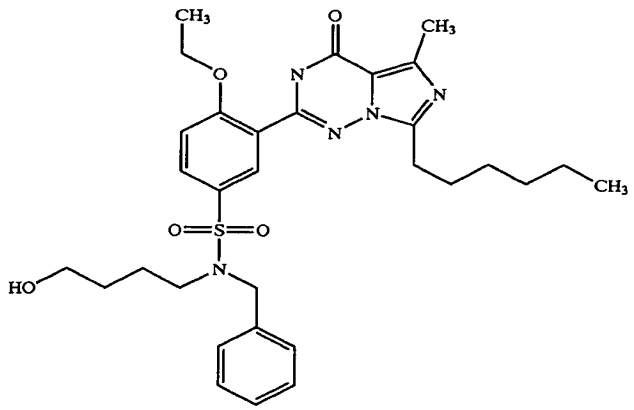
640		570.76	60	571
641		558.75	40	559
642		595.77	90	596

TABLE 1-continued

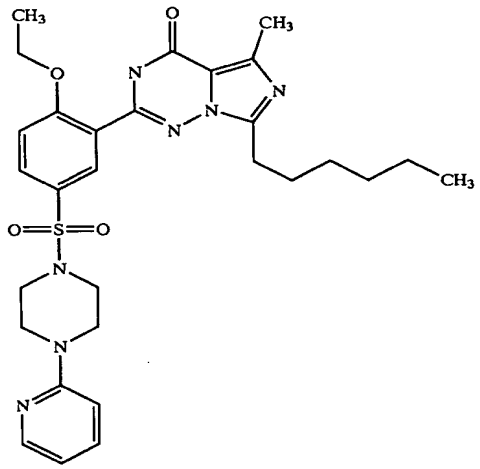
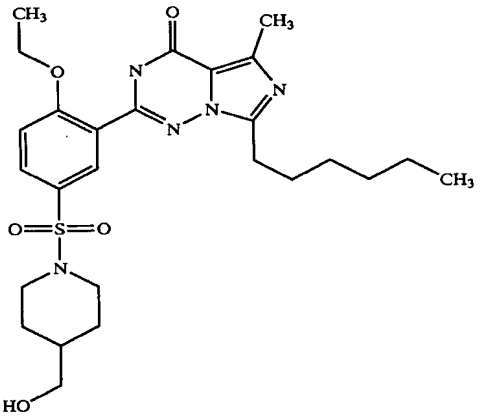
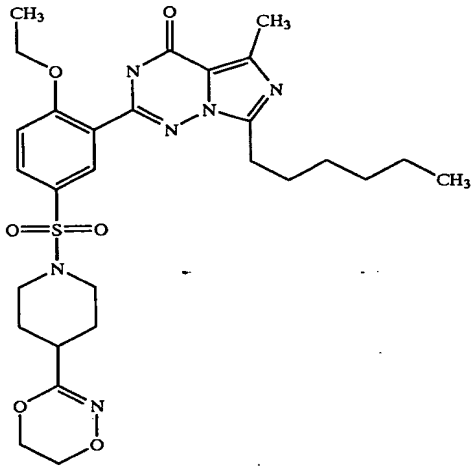
643		579.73	87	580
644		531.68	91	532
645		586.72	69	587

TABLE 1-continued

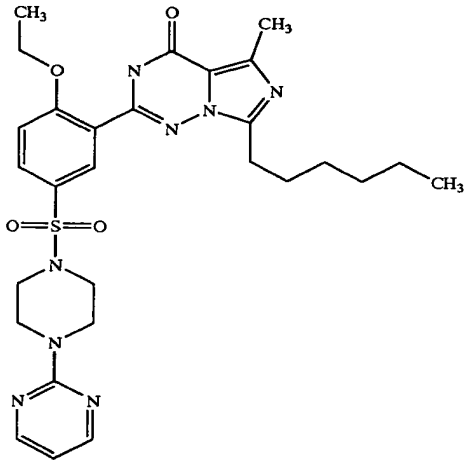
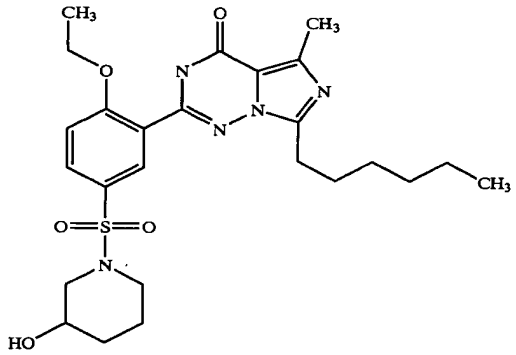
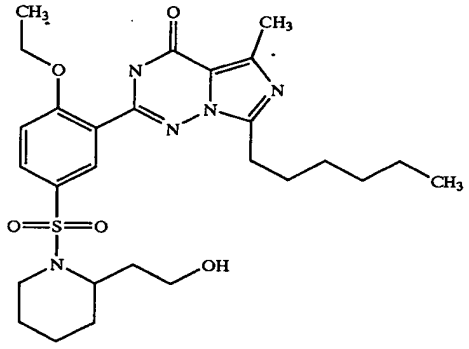
646		580.71	78	581
647		517.65	86	518
648		545.71	82	546

TABLE 1-continued

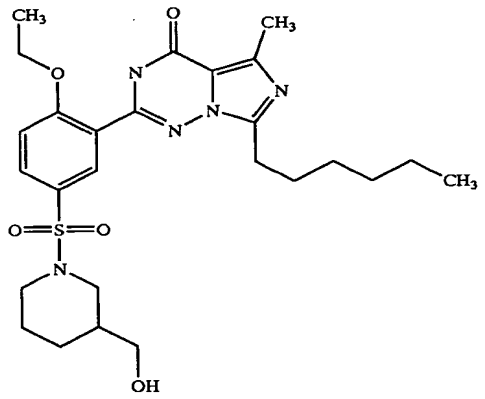
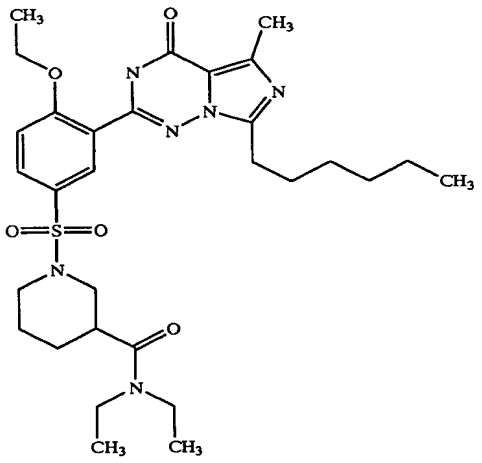
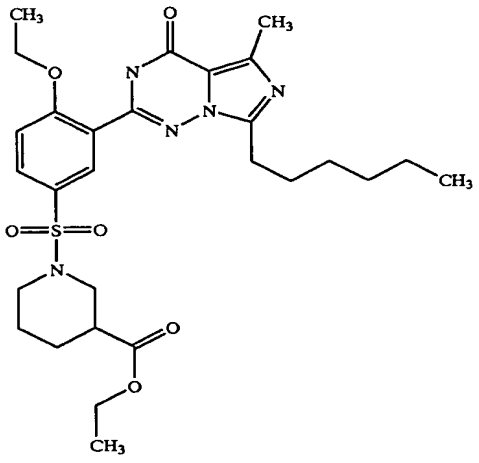
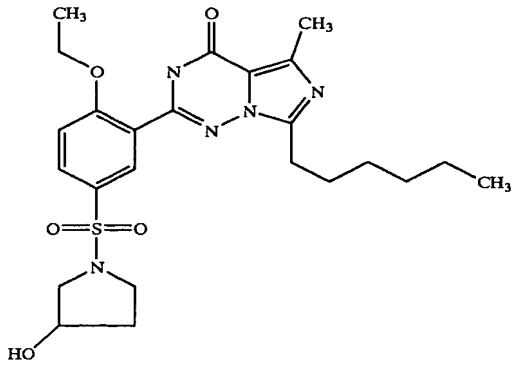
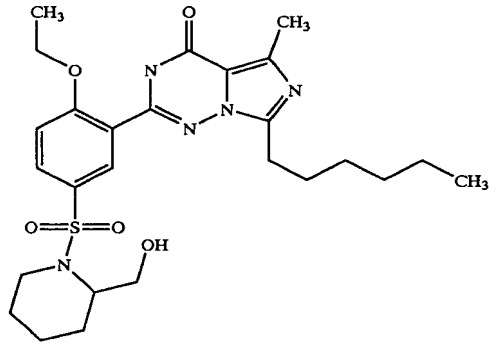
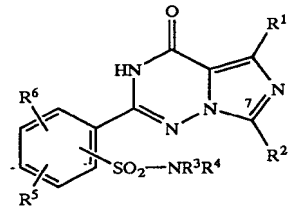
649		531.68	86	532
650		600.79	57	601
651		573.72	82	574

TABLE 1-continued

652		503.63	83	504
653		531.68	83	532

What is claimed is:

1. 7-Alkyl- and cycloalkyl-substituted imidazotriazinones of the formula (I)



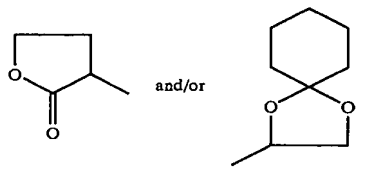
(I)

in which

R^1 represents straight-chain or branched alkyl having up to 4 carbon atoms,

R^2 represent straight-chain alkyl having at least 5 carbon atoms or branched alkyl having at least 3 carbon atoms, or represents cycloalkyl having 3 to 10 carbon atoms,

R^3 and R^4 are identical or different and represent hydrogen, or represent straight-chain or branched alkenyl having up to 8 carbon atoms, or represent a straight-chain or branched alkyl chain having up to 10 carbon atoms which is optionally interrupted by an oxygen atom and which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of trifluoromethyl, trifluoromethoxy, hydroxyl, halogen carboxyl, benzyloxycarbonyl, straight-chain or branched alkoxy, alkoxycarbonyl and alkylthio having each case up to 6 carbon atoms and/or by radicals of the formulae $—SO_3H$, $—(A)_a—NR^7R^8$, $—O—CO—NR^{7'}R^{8'}$, $—S(O)_b—R^9$, $HN=SO—R^{9'}$, $—P(O)(OR^{10})(OR^{11})$,



and/or

in which

a and b are identical or different and represent a number 0 or 1,

A represents a radical CO or SO_2,

R^7, $R^{7'}$, R^8 and $R^{8'}$ are identical or different and represent hydrogen, or represent cycloalkyl having 3 to 8 carbon atoms, aryl having 6 to 10 carbon atoms, a 5- to 6-membered unsaturated, partially unsaturated or saturated, optionally benzo-fused heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O, where the ring systems listed above are optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, nitro, trifluoromethyl, trifluoromethoxy, carboxyl, halogen, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 6 carbon atoms or by a group of the formula $—(SO_2)_c—NR^{12}R^{13}$,

in which

c represents a number 0 or 1,

R^{12} and R^{13} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 5 carbon atoms,

or

R^7, $R^{7'}$, R^8 and $R^{8'}$ represent straight-chain or branched alkoxy having up to 6 carbon atoms, or represent straight-chain or branched alkyl having up to 8 carbon atoms which is optionally mono- or polysubstituted by identical or different substituents from the group consisting of hydroxyl, halogen, aryl having from 6 to 10 carbon atoms, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 6 carbon atoms or by a group of the formula $-(CO)_d-NR^{14}R^{15}$,

in which

R^{14} and R^{15} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms,

and

d represents a number 0 or 1,

or

R^7 and R^8 and/or $R^{7'}$ and $R^{8'}$ together with the nitrogen atom form a 5- to 7-membered saturated heterocycle which may optionally contain a further heteroatom from the group consisting of S and O or a radical of the formula $-NR^{16}$,

in which

R^{16} represents hydrogen, aryl having 6 to 10 carbon atoms, or straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally substituted by hydroxyl,

R^9 and $R^{9'}$ are identical or different and represent aryl having 6 to 10 carbon atoms or benzyl, or represent straight-chain or branched alkyl having up to 4 carbon atoms,

R^{10} and R^{11} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms,

and/or the alkyl chain listed above under R^3/R^4 is optionally substituted by cycloalkyl having 3 to 8 carbon atoms, aryl having 6 to 10 carbon atoms or by a 5- to 7-membered partially unsaturated, saturated or unsaturated, optionally benzo-fused heterocycle which may contain up to 4 ring heteroatoms from the group consisting of S, N; O or a radical of the formula $-NR^{17}$, where the alkyl chain may optionally also be attached via a ring nitrogen atom,

in which

R^{17} represents hydrogen, hydroxyl, formyl, trifluoromethyl, straight-chain or branched acyl or alkoxy having in each case up to 4 carbon atoms, or represents straight-chain or branched alkyl having up to 6 carbon atoms which is optionally mono- to polysubstituted by identical or different substituents from the group consisting of hydroxyl and straight-chain or branched alkoxy having up to 6 carbon atoms,

and where aryl and the heterocycle are optionally mono- to trisubstituted by identical or different substituents from the group consisting of nitro, halogen, $-SO_3H$, straight-chain or branched monohydroxy-substituted alkyl, alkylthio or alkoxy having in each case up to 6 carbon atoms, hydroxyl, trifluoromethyl, trifluoromethoxy and/or by a radical of the formula $-(SO_2)_e-R^{18}R^{19}$,

in which

e represents a number 0 or 1,

R^{18} and R^{19} are identical or different and represent hydrogen, phenyl, benzyl or straight-chain or branched alkyl or acyl having in each case up to 6 carbon atoms,

and/or

R^3 or R^4 represent radicals of the formulae $-NR^{20}R^{21}$ or $-(O)-E-NR^{22}R^{23}$,

in which

R^{20} and R^{21} have the meaning of R^{18} and R^{19} given above and are identical to or different from this meaning, or together with the nitrogen atom form a 5- or 6-membered saturated heterocycle having a further ring heterocycle from the group consisting of S and O or a radical $-NR^{24}$,

in which

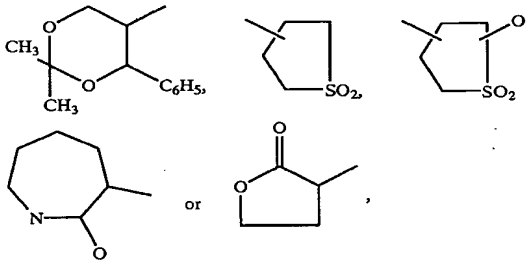
R^{24} has the meaning of R^{16} given above and is identical to or different from this meaning,

E is a straight-chain alkylene group having up to 5 carbon atoms,

R^{22} and R^{23} have the meaning of R^{18} and R^{19} given above and are identical to or different from this meaning,

and/or

R^3 or R^4 represent radicals of the formulae



or represent cycloalkyl having 3 to 8 carbon atoms, aryl having 6 to 10 carbon atoms or represent a 5- to 7-membered partially unsaturated, saturated and unsaturated, optionally benzo-fused heterocycle which may contain up to 4 heteroatoms from the group consisting of S, N; O or a radical of the formula $-NR^{25}$ which may optionally also be attached via a ring nitrogen atom,

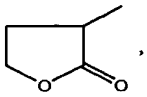
in which

R^{25} has the meaning of R^{16} given above and is identical to or different from this meaning, or represents carboxyl, formyl or straight-chain or branched acyl having up to 5 carbon atoms,

and where cycloalkyl, aryl and/or the heterocycle are optionally mono- to trisubstituted by identical or different substituents from the group consisting of halogen, trifluoromethyl, trifluoromethoxy, carboxyl, straight-chain or branched acyl or alkoxycarbonyl having in each case up to 6 carbon atoms, nitro and/or by groups of the formulae $-SO_3H$, $-OR^{26}$, $(SO_2)_fNR^{27}R^{28}$, $-P(O)(OR^{29})(OR^{30})$,

in which

R^{26} represents a radical of the formula



represents cycloalkyl having 3 to 7 carbon atoms, or hydrogen or straight-chain or branched alkyl having up to 5 carbon atoms which is optionally substituted by cycloalkyl having 3 to 7 carbon atoms, straight-

chain or branched alkoxy or alkoxycarbonyl having in each case up to 6 carbon atoms, hydroxyl, carboxyl or phenyl, which for its part may be mono- to trisubstituted by identical or different substituents from the group consisting of straight-chain or branched alkoxy having up to 4 carbon atoms, hydroxyl and halogen,

f is a number 0 or 1,

R^{27} and R^{28} have the meaning of R^{18} and R^{19} given above and are identical to or different from this meaning or represent a radical of the formula $—CO—NH_2$,

R^{29} and R^{30} have the meaning of R^{10} and R^{11} given above and are identical to or different from this meaning,

and/or cycloalkyl, aryl and/or the heterocycle are optionally substituted by straight-chain or branched alkyl having up to 6 carbon atoms which is optionally substituted by hydroxyl, carboxyl, by a 5- to 7-membered heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O or by groups of the formulae $—SO_2—R^{31}$, $P(O)(OR^{32})(OR^{33})$ or $—NR^{34}R^{35}$,

in which

R^{31} is hydrogen or has the meaning of R^9 given above and is identical to or different from this meaning,

R^{32} and R^{33} have the meaning of R^{10} and R^{11} given above and are identical to or different from this meaning,

R^{34} and R^{35} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms which is optionally substituted by hydroxyl or straight-chain or branched alkoxy having up to 4 carbon atoms, or

R^{34} and R^{35} together with the nitrogen atom form a 5- to 6-membered saturated heterocycle which may contain a further heteroatom from the group consisting of S and O or a radical of the formula $—NR^{36}$,

in which

R^{36} has the meaning of R^{16} given above and is identical to or different from this meaning,

or

R^3 and R^4 together with the nitrogen atom form a 5- to 7-membered unsaturated or saturated or partially unsaturated, optionally benzo-fused heterocycle which may optionally contain up to 3 heteroatoms from the group consisting of S, N, O or a radical of the formula $—NR^{37}$,

in which

R^{37} represents hydrogen, hydroxyl, formyl, trifluoromethyl, straight-chain or branched acyl, alkoxy or alkoxycarbonyl having in each case up to 4 carbon atoms, or represents cycloalkyl having 3 to 8 carbon atoms, or represents straight-chain or branched alkyl having up to 6 carbon atoms which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, trifluoromethyl, pyridyl, carboxyl, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 6 carbon atoms,

or

R^{37} represents a radical of the formula $—(CO)_g—G$,

in which

g represents a number 0 or 1,

G represents aryl having 6 to 10 carbon atoms or a 5- to 6-membered aromatic heterocycle having up to 4 heteroatoms from the group consisting of S, N and/or O, where the ring systems listed above are optionally mono- to trisubstituted by identical or different substituents from the group consisting of halogen, straight-chain or branched alkoxy, alkyl or alkylthio having in each case up to 6 carbon atoms, hydroxyl and trifluoromethyl,

and the heterocycle mentioned under R^3 and R^4, formed via the nitrogen, is optionally mono- to trisubstituted, optionally also geminally, by identical or different substituents from the group consisting of hydroxyl, formyl, carboxyl, straight-chain or branched acyl and alkoxycarbonyl having in each case up to 6 carbon atoms and groups of the formulae $—P(O)(OR^{38})(OR^{39})$ and $—(CO)_g—NR^{40}R^{41}$,

in which

R^{38} and R^{39} have the meaning of R^{10} and R^{11} given above and are identical to or different from this meaning,

g represents a number 0 or 1,

and

R^{40} and R^{41} are identical or different and have the meaning of R^{18} and R^{19} given above,

and/or the heterocycle mentioned under R^3 and R^4, formed via the nitrogen, is optionally substituted by straight-chain or branched alkyl having up to 6 carbon atoms which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, halogen, carboxyl, cycloalkyl or cycloalkyloxy having in each case 3 to 8 carbon atoms, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 6 carbon atoms or by a radical of the formula $—SO_3H$, $—NR^{42}R^{43}$ or $P(O)OR^{44}OR^{45}$,

in which

R^{42} and R^{43} are identical or different and represent hydrogen, phenyl, carboxyl, benzyl or straight-chain or branched alkyl or alkoxy having in each case up to 6 carbon atoms,

R^{44} and R^{45} are identical or different and have the meaning of R^{10} and R^{11} given above,

and/or the alkyl is optionally substituted by benzyloxy or aryl having 6 to 10 carbon atoms, which for its part may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, hydroxyl, straight-chain or branched alkoxy or alkylthio having in each case up to 6 carbon atoms, or by a group of the formula $—NR^{42'}R^{43'}$,

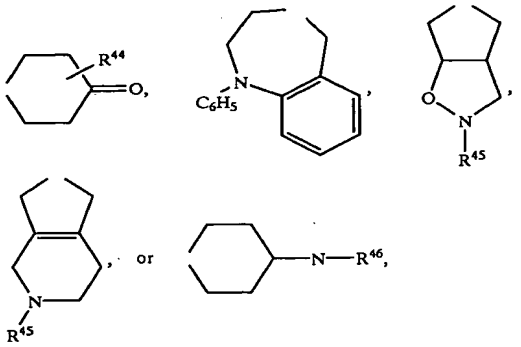
in which

$R^{42'}$ and $R^{43'}$ have the meaning of R^{42} and R^{43} given above and are identical to or different from this meaning,

and/or the heterocycle mentioned under R^3 and R^4, formed via a nitrogen atom, is optionally substituted by aryl having 6 to 10 carbon atoms or by a 5- to 7-membered saturated, partially unsaturated or unsaturated heterocycle having up to 3 ring heteroatoms from the group consisting of S, N and/or O, optionally also attached via an N function, where the ring systems for their part may be substituted by halogen, hydroxyl or by straight-chain or branched alkyl, alkylthio or alkoxy having in each case up to 6 carbon atoms,

or

R^3 and R^4 together with the nitrogen atom form radicals of the formulae



in which

R^{44} represents hydrogen or straight-chain or branched alkyl or alkoxycarbonyl having in each case up to 6 carbon atoms,

R^{45} and $R^{45'}$ are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms,

R^{46} represents hydroxyl or straight-chain or branched alkoxy having up to 6 carbon atoms,

R^5 and R^6 are identical or different and represent hydrogen, straight-chain or branched alkyl having up to 6 carbon atoms, hydroxy or represents straight-chain or branched alkoxy having up to 6 carbon atoms,

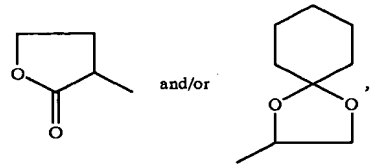
or their salts or stereoisomeric forms.

2. Compounds of the formula (I) according to claim 1, in which

R^1 represents straight-chain or branched alkyl having up to 3 carbon atoms,

R^2 represents straight-chain alkyl having 5 to 15 carbon atoms or branched alkyl having 3 to 15 carbon atoms, or represents cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl or cyclooctyl,

R^3 and R^4 are identical or different and represent hydrogen, or represent straight-chain or branched alkenyl having up to 4 carbon atoms, or represent a straight-chain or branched alkyl chain having up to 6 carbon atoms which is optionally interrupted by an oxygen atom and which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, carboxyl, straight-chain or branched alkoxy, alkoxycarbonyl and alkylthio having in each case up to 4 carbon atoms and/or by radicals of the formulae $-SO_3H$, $-(A)_a-NR^7R^8$, $-O-CO-NR^{7'}R^{8'}$, $-S(O)_b-R^9$, $HN=SO-R^{9'}$, $-P(O)(OR^{10})(OR^{11})$,



in which

a and b are identical or different and represent a number 0 or 1,

A represents a radical CO or SO_2,

R^7, $R^{7'}$, R^8 and $R^{8'}$ are identical or different and represent hydrogen, or represent phenyl, naphthyl, or pyridyl, where the ring systems listed above are optionally mono- to disubstituted by identical or different substituents from the group consisting of hydroxyl, nitro, trifluoromethyl, trifluoromethoxy, carboxyl, halogen, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 4 carbon atoms, or represent straight-chain or branched alkoxy having up to 4 carbon atoms, or represent straight-chain or branched alkyl having up to 6 carbon atoms which is optionally mono- or polysubstituted by identical or different substituents from the group consisting of hydroxyl, fluorine, chlorine, bromine, phenyl, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 4 carbon atoms or by a group of the formula $-(CO)_d-NR^{14}R^{15}$,

in which

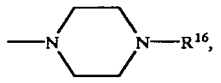
R^{14} and R^{15} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms,

and

d represents a number 0 or 1,

or

R^7 and R^8 and/or $R^{7'}$ and $R^{8'}$ together with the nitrogen atom form a pyrrolidinyl, piperidinyl or morpholinyl ring or a radical of the formula



in which

R^{16} represents hydrogen, phenyl, naphthyl or straight-chain or branched alkyl having up to 4 carbon atoms, which is optionally substituted by hydroxyl,

R^9 and $R^{9'}$ are identical or different and represent phenyl or benzyl, or represent straight-chain or branched alkyl having up to 3 carbon atoms,

R^{10} and R^{11} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms,

and/or the alkyl chain mentioned above under R^3/R^4 is optionally substituted by phenyl, naphthyl, morpholinyl, pyridyl, tetrahydropyranyl, tetrahydrofuranyl or thienyl, where the radical may optionally also be attached to the alkyl chain via a ring nitrogen atom,

and where aryl and the heterocycle are optionally mono- to disubstituted by identical or different substituents from the group consisting of nitro, fluorine, chlorine, bromine, $-SO_3H$, straight-chain or branched monohydroxy-substituted alkyl, alkylthio or alkoxy having in each case up to 4 carbon atoms, hydroxyl, trifluoromethyl, trifluoromethoxy and/or by a radical of the formula $-(SO_2)_e-NR^{18}R^{19}$,

in which

e represents a number 0 or 1,

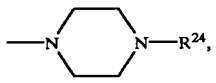
R^{18} and R^{19} are identical or different and represent hydrogen, phenyl, benzyl or straight-chain or branched alkyl or acyl having in each case up to 4 carbon atoms,

and/or

R^3 and R^4 represent radicals of the formulae $-NR^{20}R^{21}$ or $-(O)-E-NR^{22}R^{23}$,

in which

R^{20} and R^{21} have the meaning of R^{18} and R^{19} given above and are identical to or different from this meaning, or together with the nitrogen atom form a morpholinyl ring, pyrrolidinyl ring or a radical of the formula



in which

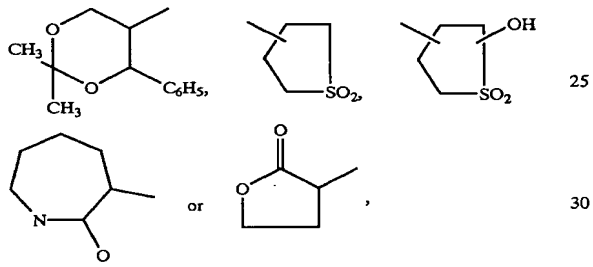
R^{24} has the meaning of R^{16} given above and is identical to or different from this meaning,

E represents a straight-chain alkylene group having up to 4 carbon atoms,

R^{22} and R^{23} have the meaning of R^{18} and R^{19} given above and are identical to or different from this meaning,

and/or

R^3 or R^4 represent radicals of the formulae

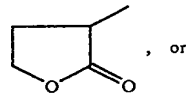


or represent cyclopentyl, cyclohexyl, naphthyl, phenyl, pyridyl, or quinolyl or tetrazolyl attached via the phenyl ring,

and where the ring systems given above are optionally mono- to disubstituted by identical or different substituents from the group consisting of fluorine, chlorine, trifluoromethyl, trifluoromethoxy, carboxyl, straight-chain or branched acyl and alkoxycarbonyl having in each case up to 4 carbon atoms and/or by groups of the formulae $—SO_3H$, $—OR^{26}$, $(SO_2)_fNR^{27}R^{28}$, $—P(O)(OR^{29})(OR^{30})$,

in which

R^{26} represents a radical of the formula



represents cyclopentyl or cyclohexyl, or represents hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms which is optionally substituted by straight-chain or branched alkoxy or alkoxycarbonyl having in each case up to 4 carbon atoms, hydroxyl, carboxyl or phenyl, which for its part may be mono- to disubstituted by identical or different substituents from the group consisting of straight-chain or branched alkoxy having up to 3 carbon atoms, hydroxyl and halogen,

f represents a number 0 or 1,

R^{27} and R^{28} have the meaning of R^{18} an R^{19} given above and are identical to or different from this meaning or represent a radical of the formula $—CO—NH_2$,

R^{29} and R^{30} have the meaning of R^{10} and R^{11} given above and are identical to or different from this meaning,

and/or the ring systems given above are optionally substituted by straight-chain or branched alkyl having up to 4 carbon atoms, which are optionally substituted by hydroxyl, carboxyl, morpholine, pyridyl or by groups of the formula $—SO_2—R^{31}$, $P(O)(OR^{32})(OR^{33})$ or $—NR^{34}R^{35}$,

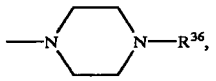
in which

R^{31} represents hydrogen or has the meaning of R^9 given above and is identical to or different from this meaning,

R^{32} and R^{33} have the meaning of R^{10} and R^{11} given above and are identical to or different from this meaning,

R^{34} and R^{35} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms which is optionally substituted by hydroxyl or straight-chain or branched alkoxy having up to 3 carbon atoms, or

R^{34} and R^{35} together with the nitrogen atom form a morpholinyl, pyrrolidinyl, piperidinyl ring or a radical of the formula

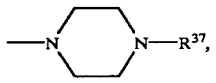


in which

R^{36} has the meaning of R^{16} given above and is identical to or different from this meaning,

or

R^3 and R^4 together with the nitrogen atom form a piperidinyl, pyrrolidinyl or morpholinyl ring, or a radical of the formula



in which

R^{37} represents hydrogen, hydroxyl, formyl, trifluoromethyl, straight-chain or branched acyl, alkoxy or alkoxycarbonyl having in each case up to 4 carbon atoms, or represents cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl, or represents straight-chain or branched alkyl having up to 4 carbon atoms which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, trifluoromethyl, pyridyl, carboxyl, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 4 carbon atoms,

or

R^{37} represents a radical of the formula $—(CO)_g—G$,

in which

g represents a number 0 or 1,

G represents naphthyl, phenyl, pyridyl or pyrimidyl, where the ring systems listed above are optionally mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, straight-chain or branched alkoxy, alkyl or alkylthio having in each case up to 4 carbon atoms, hydroxyl and trifluoromethyl,

and the heterocycles listed above under R^3 and R^4 are optionally mono- to trisubstituted, optionally also geminally, by identical or different substituents from the group consisting of hydroxyl, formyl, carboxyl, straight-chain or branched acyl or alkoxycarbonyl having in each case up to 4 carbon atoms and groups of the formulae $—P(O)(OR^{38})(OR^{39})$ or $—(CO)_g—NR^{40}R^{41}$,

in which

R^{38} and R^{39} have the meaning of R^{10} and R^{11} given above and are identical to or different from this meaning,

g represents a number 0 or 1,

and

R^{40} and R^{41} are identical or different and have the meaning of R^{18} and R^{19} given above,

and/or the heterocycles listed under R^3 and R^4 are optionally substituted by straight-chain or branched alkyl having up to 4 carbon atoms which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, fluorine, chlorine, carboxyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclopentyloxy, cyclohexyloxy, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 4 carbon atoms or by a radical of the formula $—SO_3H$, $—NR^{42}R^{43}$ or $P(O)OR^{44}OR^{45}$,

in which

R^{42} and R^{43} are identical or different and represent hydrogen, phenyl, carboxyl, benzyl or straight-chain or branched alkyl or alkoxy having in each case up to 4 carbon atoms,

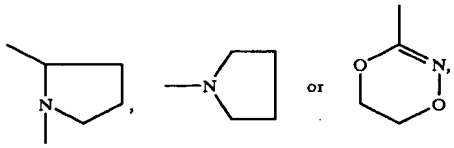
R^{44} and R^{45} are identical or different and have the meaning of R^{10} and R^{11} given above,

and/or the alkyl is optionally substituted by benzyloxy, naphtyl or phenyl, which for its part may be mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, hydroxyl, straight-chain or branched alkoxy and alkylthio having in each case up to 4 carbon atoms, or by a group of the formula $—NR^{42'}R^{43'}$,

in which

$R^{42'}$ and $R^{43'}$ have the meaning of R^{42} and R^{43} given above and are identical to or different from this meaning,

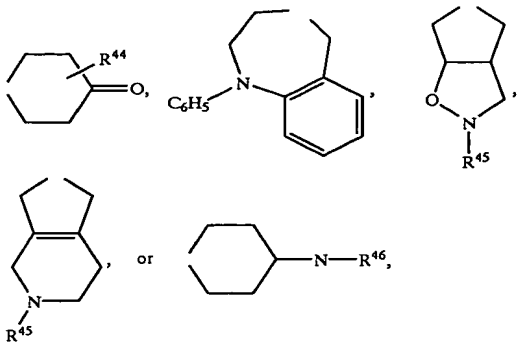
and/or the heterocycles listed under R^3 and R^4 are optionally substituted by phenyl, naphthyl or by radicals of the formulae



where the ring systems for their part may be substituted by fluorine, chlorine, hydroxyl or by straight-chain or branched alkyl, alkylthio or alkoxy having in each case up to 4 carbon atoms,

or

R^3 and R^4 together with the nitrogen atom form radicals of the formulae



in which

R^{44} represents hydrogen or straight-chain or branched alkyl or alkoxycarbonyl having in each case up to 3 carbon atoms,

R^{45} and $R^{45'}$ are identical or different arid represent hydrogen or methyl,

R^{46} represents hydroxyl or straight-chain or branched alkoxy having up to 4 carbon atoms,

R^5 and R^6 are identical or different and represent hydrogen, straight-chain or branched alkyl having up to 4 carbon atoms, hydroxyl or represent straight-chain or branched alkoxy having up to 4 carbon atoms,

or their salts or stereoisomeric forms.

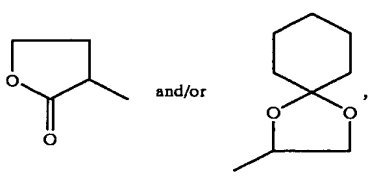
3. Compounds of the formula (I) according to claim 1,

in which

R^1 represents straight-chain or branched alkyl having up to 3 carbon atoms,

R^2 represents straight-chain alkyl having 5 to 12 carbon atoms or branched alkyl having 3 to 12 carbon atoms, or represents cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl or cyclooctyl,

R^3 and R^4 are identical or different and represent hydrogen, or represent straight-chain or branched alkenyl having up to 4 carbon atoms, or represent a straight-chain or branched alkyl chain having up to 6 carbon atoms which is optionally interrupted by an oxygen atom and which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, carboxyl, straight-chain or branched alkoxy, alkoxycarbonyl and alkylthio having in each case up to 4 carbon atoms and/or by radicals of the formulae $—SO_3H$, $—(A)_a—NR^7R^8$, $—O—CO—NR^{7'}R^{8'}$, $—S(O)_b—R^9$, $HN═SO—R^{9'}$, $—P(O)(OR^{10})(OR^{11})$,



in which

a and b are identical or different and represent a number 0 or 1,

A represents a radical CO or SO_2,

R^7, $R^{7'}$, R^8 and $R^{8'}$ are identical or different and represent hydrogen, or represent phenyl, naphthyl, or

pyridyl, where the ring systems listed above are optionally mono- to disubstituted by identical or different substituents from the group consisting of hydroxyl, nitro, trifluoromethyl, trifluoromethoxy, carboxyl, halogen, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 4 carbon atoms, or represent straight-chain or branched alkoxy having up to 4 carbon atoms, or represent straight-chain or branched alkyl having up to 6 carbon atoms which is optionally mono- or polysubstituted by identical or different substituents from the group consisting of hydroxyl, fluorine, chlorine, bromine, phenyl, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 4 carbon atoms or by a group of the formula $—(CO)_d—NR^{14}R^{15}$,

in which

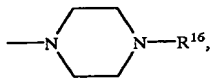
R^{14} and R^{15} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms,

and

d represents a number 0 or 1,

and

R^7 and R^8 and/or $R^{7'}$ and $R^{8'}$ together with the nitrogen atom form a pyrrolidinyl, piperidinyl or morpholinyl ring or a radical of the formula



in which

R^{16} represents hydrogen, phenyl, naphthyl or straight-chain or branched alkyl having up to 4 carbon atoms which is optionally substituted by hydroxyl,

R^9 and $R^{9'}$ are identical or different and represent phenyl or benzyl, or represent straight-chain or branched alkyl having up to 3 carbon atoms,

R^{10} and R^{11} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms,

and/or the alkyl chain listed above under R^3/R^4 is optionally substituted by phenyl, naphthyl, morpholinyl, pyridyl, tetrahydropyranyl, tetrahydrofuranyl or thienyl, where the attachment to the alkyl chain may optionally also take place via a ring nitrogen atom,

and where aryl and the heterocycle are optionally mono- to disubstituted by identical or different substituents from the group consisting of nitro, fluorine, chlorine, bromine, $—SO_3H$, straight-chain or branched monohydroxy-substituted alkyl, alkylthio or alkoxy having in each case up to 4 carbon atoms, hydroxyl, trifluoromethyl, trifluoromethoxy and/or by a radical of the formula $—(SO_2)_e—NR^{18}R^{19}$,

in which

e represents a number 0 or 1,

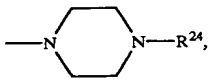
R^{18} and R^{19} are identical or different and represent hydrogen, phenyl, benzyl or straight-chain or branched alkyl or acyl having in each case up to 4 carbon atoms,

and/or

R^3 or R^4 represents radicals of the formulae $—NR^{20}R^{21}$ or $—(O)—E—NR^{22}R^{23}$,

in which

R^{20} and R^{21} have the meaning of R^{18} and R^{19} given above and are identical to or different from this meaning, or together with the nitrogen atom form a morpholinyl ring, pyrrolidinyl ring or a radical of the formula



in which

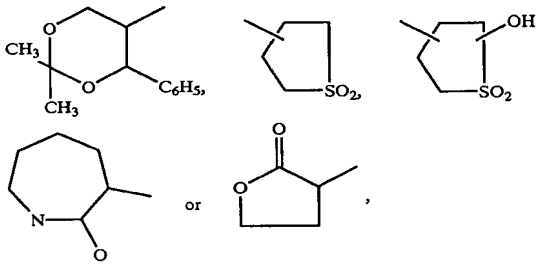
R^{24} has the meaning of R^{16} given above and is identical to or different from this meaning,

E represents a straight-chain alkylene group having up to 4 carbon atoms,

R^{22} and R^{23} have the meaning of R^{18} and R^{19} given above and are identical to or different from this meaning

and/or

R^3 or R^4 represent the radicals of the formulae

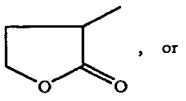


or represent cyclopentyl, cyclohexyl, naphthyl, phenyl, pyridyl, or quinolinyl or tetrazolyl attached via the phenyl ring,

and where the ring systems given above are optionally mono- to disubstituted by identical or different substituents from the group consisting of fluorine, chlorine, trifluoromethyl, trifluoromethoxy, carboxyl, straight-chain or branched acyl and alkoxycarbonyl having in each case up to 4 carbon atoms and/or by groups of the formulae $—SO_3H$, $—OR^{26}$, $(SO_2)_fNR^{27}R^{28}$, $—P(O)(OR^{29})(OR^{30})$,

in which

R^{26} represents a radical of the formula



represents cyclopentyl or cyclohexyl, or represents hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms which is optionally substituted by straight-chain or branched alkoxy or alkoxycarbonyl having in each case up to 4 carbon atoms, hydroxyl, carboxyl or phenyl, which for its part may be mono- to disubstituted by identical or different substituents from the group consisting of straight-chain or branched alkoxy having up to 3 carbon atoms, hydroxyl and halogen,

f represents a number 0 or 1,

R^{27} and R^{28} have the meaning of R^{18} and R^{19} given above and are identical to or different from this meaning or represent a radical of the formula $—CO—NH_2$,

R^{29} and R^{30} have the meaning of R^{10} arid R^{11} given above and are identical to or different from this meaning,

and/or the ring systems given above are optionally substituted by straight-chain or branched alkyl having up to 4 carbon atoms which are optionally substituted by hydroxyl, carboxyl, morpholine, pyridyl or by groups of the formula $—SO_2—R^{31}$, $P(O)(OR^{32})(OR^{33})$ or $—NR^{34}R^{35}$,

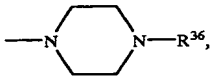
in which

R^{31} represents hydrogen or has the meaning of R^9 given above and is identical to or different from this meaning,

R^{32} and R^{33} have the meaning of R^{10} and R^{11} given above and are identical to or different from this meaning,

R^{34} and R^{35} are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms which is optionally substituted by hydroxyl or straight-chain or branched alkoxy having up to 3 carbon atoms, or

R^{34} and R^{35} together with the nitrogen atom form a morpholinyl, pyrrolidinyl, piperidinyl ring or a radical of the formula

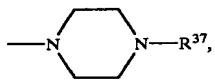


in which

R^{36} has the meaning of R^{16} given above and is identical to or different from this meaning,

or

R^3 and R^4 together with the nitrogen atom form a piperidinyl, pyrrolidinyl or morpholinyl ring, or a radical of the formula



in which

R^{37} represents hydrogen, hydroxyl, formyl, trifluoromethyl, straight-chain or branched acyl, alkoxy or alkoxycarbonyl having in each case up to 4 carbon atoms, or represents cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl, or represents straight-chain or branched alkyl having up to 4 carbon atoms which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, trifluoromethyl, pyridyl, carboxyl, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 4 carbon atoms,

or

R^{37} represents a radical of the formula $—(CO)_g—G$,

in which

g represents a number 0 or 1,

G represents naphthyl, phenyl, pyridyl or pyrimidyl, where the ring systems listed above are optionally mono- to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, straight-chain or branched alkoxy, alkyl or alkylthio having in each case up to 4 carbon atoms, hydroxyl and trifluoromethyl,

and the heterocycles listed under R^3 and R^4 are optionally mono- to trisubstituted, optionally also geminally, by identical or different substituents from the group consisting of hydroxyl, formyl, carboxyl, straight-chain or branched acyl or alkoxycarbonyl having in each case up to 4 carbon atoms and groups of the formulae $—P(O)(OR^{38})(OR^{39})$ or $—(CO)_g—NR^{40}R^{41}$,

in which

R^{38} and R^{39} have the meaning of R^{10} and R^{11} given above and are identical to or different from this meaning,

g represents a number 0 or 1,

and

R^{40} and R^{41} are identical or different and have the meaning of R^{18} and R^{19} given above,

and/or the heterocycles listed under R^3 and R^4 are optionally substituted by straight-chain or branched alkyl having up to 4 carbon atoms which is optionally mono- to trisubstituted by identical or different substituents from the group consisting of hydroxyl, fluorine, chlorine, carboxyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cyclopentyloxy, cyclohexyloxy, straight-chain or branched alkoxy and alkoxycarbonyl having in each case up to 4 carbon atoms or by a radical of the formula $—SO_3H$, $—NR^{42}R^{43}$ or $P(O)OR^{44}OR^{45}$,

in which

R^{42} and R^{43} are identical or different and represent hydrogen, phenyl, carboxyl, benzyl or straight-chain or branched alkyl or alkoxy having in each case up to 4 carbon atoms,

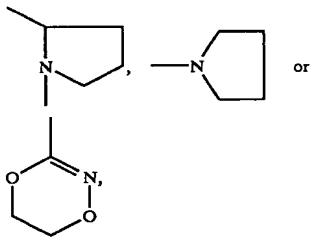
R^{44} and R^{45} are identical or different and have the meaning of R^{10} and R^{11} given above,

and/or the alkyl is optionally substituted by benzyloxy, naphtyl or phenyl, which for its part may be mono to trisubstituted by identical or different substituents from the group consisting of fluorine, chlorine, hydroxyl, straight-chain or branched alkoxy or alkylthio having in each case up to 4 carbon atoms, or by a group of the formula $—NR^{42'}R^{43'}$

in which

$R^{42'}$ and $R^{43'}$ have the meaning of R^{42} and R^{43} given above and are identical to or different from this meaning,

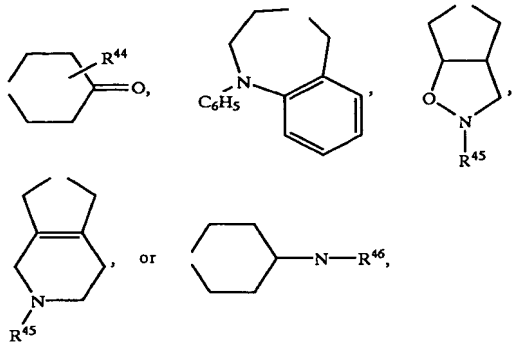
and/or the heterocycles listed under R^3 and R^4 are optionally substituted by phenyl, naphthyl or by radicals of the formulae



where the ring systems for their part may be substituted by fluorine, chlorine, hydroxyl or by straight-chain or branched alkyl, alkylthio or alkoxy having in each case up to 4 carbon atoms,

or

R^3 and R^4 together with the nitrogen atom form radicals of the formulae



in which

R^{44} represents hydrogen or straight-chain or branched alkyl or alkoxycarbonyl having in each case up to 3 carbon atoms,

R^{45} and $R^{45'}$ are identical or different and represent hydrogen or methyl,

R^{46} represents hydroxyl or straight-chain or branched alkoxy having up to 4 carbon atoms,

R^5 and R^6 are identical or different and represent hydrogen, straight-chain or branched alkyl having up to 4 carbon atoms, hydroxyl or represent straight-chain or branched alkoxy having up to 4 carbon atoms,

or their salts or stereoisomeric forms.

4. Compounds of the general formula (I) according to claim 1,

in which

R^1 represents methyl or ethyl,

R^2 represents straight-chain alkyl having 5 to 11 carbon atoms or branched alkyl having 3 to 11 carbon atoms, or represents cyclopentyl, cyclohexyl, cycloheptyl,

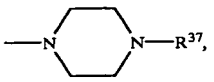
R^3 and R^4 are identical or different and represent straight-chain or branched alkyl having up to 4 carbon atoms which is optionally substituted by hydroxyl, morpholinyl, methoxy, ethoxy, N,N-dimethylamino, N,N-diethylamine or phenyl, which for its part may be substituted up to 3 times by identical or different substituents from the group consisting of methoxy, or represents cyclopropyl, or or represents phenyl which is optionally substituted up to 3 times by identical or different substituents from the group consisting of fluorine, chlorine or hydroxyl, methoxy, ethoxy, fluorine or by straight-chain or branched alkyl having up to 3 carbon atoms, which for its part may be substituted by hydroxyl,

or

R^3 and R^4 together with the nitrogen atom form a morpholinyl, pyrrolidinyl or piperidinyl ring which are optionally substituted by hydroxyl or by radicals of the formulae $—P(O)(OC_2H_5)_2$ or $—CH_2—P(O)OH(OC_2H_5)$ or by straight-chain or branched alkyl having up to 3 carbon atoms, which for its part may be substituted by hydroxyl or methoxy, or

or

R^3 and R^4 together with the nitrogen atom form a radical of the formula



in which

R^{37} represents pyrimidyl, ethoxycarbonyl or a radical of the formula $—CH_2—P(O)(OCH_3)_2$ or represents straight-chain or branched alkyl having up to 3 carbon atoms which is optionally substituted by hydroxyl or methoxy,

R^5 represents hydrogen,

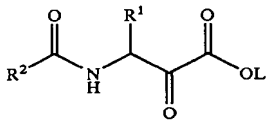
and

R^6 represents ethoxy,

or their salts or stereoisomeric forms.

5. Process for preparing compounds of the general formula (I) according to claim 1, characterized in that

initially compounds of the general formula (II)



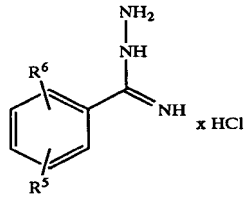
(II)

in which

R^1 and R^2 are as defined above in claim 1,

and

L represents straight-chain or branched alkyl having up to 4 carbon atoms, are converted with compounds of the general formula (III)

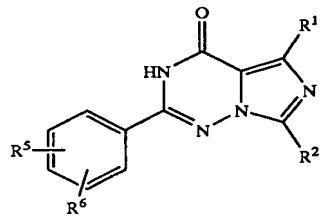


(III)

in which

R^5 and R^6 are as defined above in claim 1,

in a two-step reaction, first using the system consisting of ethanol and then using the system consisting of phosphorus oxytrichloride/dichloroethane, into the compounds of the formula (IV)

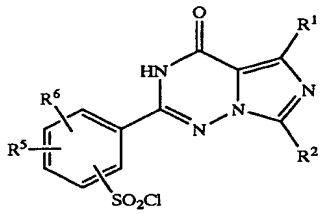


(IV)

in which

R^1, R^2, R^5 and R^6 are as defined above in claim 1,

in a further step reacted with chlorosulphonic acid to give the compounds of the formula (V)



(V)

in which

R^1, R^2, R^5 and R^6 are as defined above in claim **1**, and then reacted with amines of the formula (VI)

$$HN^3R^4 \quad \text{(VI)}$$

in which

R^3 and R^4 are as defined above in claim **1**, in inert solvents.

6. Medicaments, comprising a compound of the general formula (I) according to claim **1** and pharmaceutically acceptable auxiliaries and/or excipients.

7. A method of treating a disease or condition mediated by a cGMP-metabolizing phosphodiesterase, comprising administering to a mammal an effective amount of a compound of claim **1**.

8. A method of treating a cardiovascular disorder in a mammal, comprising administering an effective amount of a compound of claim **1**.

9. A method of relaxing smooth muscles, comprising administering to a mammal an effective amount of a compound of claim **1**.

10. A method of treating female sexual dysfunction in a mammal, comprising administering an effective amount of a compound of claim **1**.

11. A method of treating erectile dysfunction in a mammal, comprising administering an effective amount of a compound of claim **1**.

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